Annual Report
2006-2007

IICB

भारतीय रासायनिक जीवविज्ञान संस्थान
Indian Institute of Chemical Biology

IICB
Annual Report
2006-2007

Indian Institute of Chemical Biology

(A Unit of Council of Scientific & Industrial Research)
4, Raja S. C. Mullick Road
Kolkata - 700 032
India

CONTENTS

From Director's Desk

I would like to express immense pleasure in presenting the Annual Report of this Institute for the period from April 2006 to March 2007. Every year the Institute publishes its Annual Report to disseminate a brief description of our research activities particularly based on published works and patents to our friends, well wishers and scientific communities across the globe. Apart from the scientific contributions, this report also includes critical information about our infrastructure, extramural funding, intellectual property and other various aspects of scientific management and administration.

The growth of an Institute, resembling ours, essentially depends on its R&D activities and IICB, like preceding years, continued its progress through quality science. We have offered substantial attention in developing drug from our indigenous and natural resources like native Indian plants. The chemistry division achieved major success by isolating bioactive molecules from medicinal plants. This division has formulated a herbal composition for the treatment of prostate cancer. The molecular and human genetics division has identified a large protein complex from Leishmania parasites having potency to correct respiratory defects due to mitochondrial mutations that occur in certain human genetic disorders and the work was published in 'Science'. This division is also engaged in research on molecular basis of head and neck cancer (HNSCC), Haemophilia, Glaucoma, Wilson disease etc and studying various aspects of Vibrio cholerae genes and their role in pathogenesis. The infectious disease and immunology division is involved in research on fields of Leishmaniasis and Cholera. The cell biology and physiology division is engaged in understanding physiology, pathophysiology and mechanism of certain metabolic and degenerative diseases. The drug development, diagnostics & biotechnology division is involved in biological research to promote development of new products, processes and technologies of commercial and industrial importance from plants and venoms whereas the structural biology & bio-informatics division is engaged in research on structural characterization of potentially important biological macromolecules and other small molecules of therapeutic interest against various diseases like tuberculosis, leishmaniasis, cholera, cancer, diabetes etc.

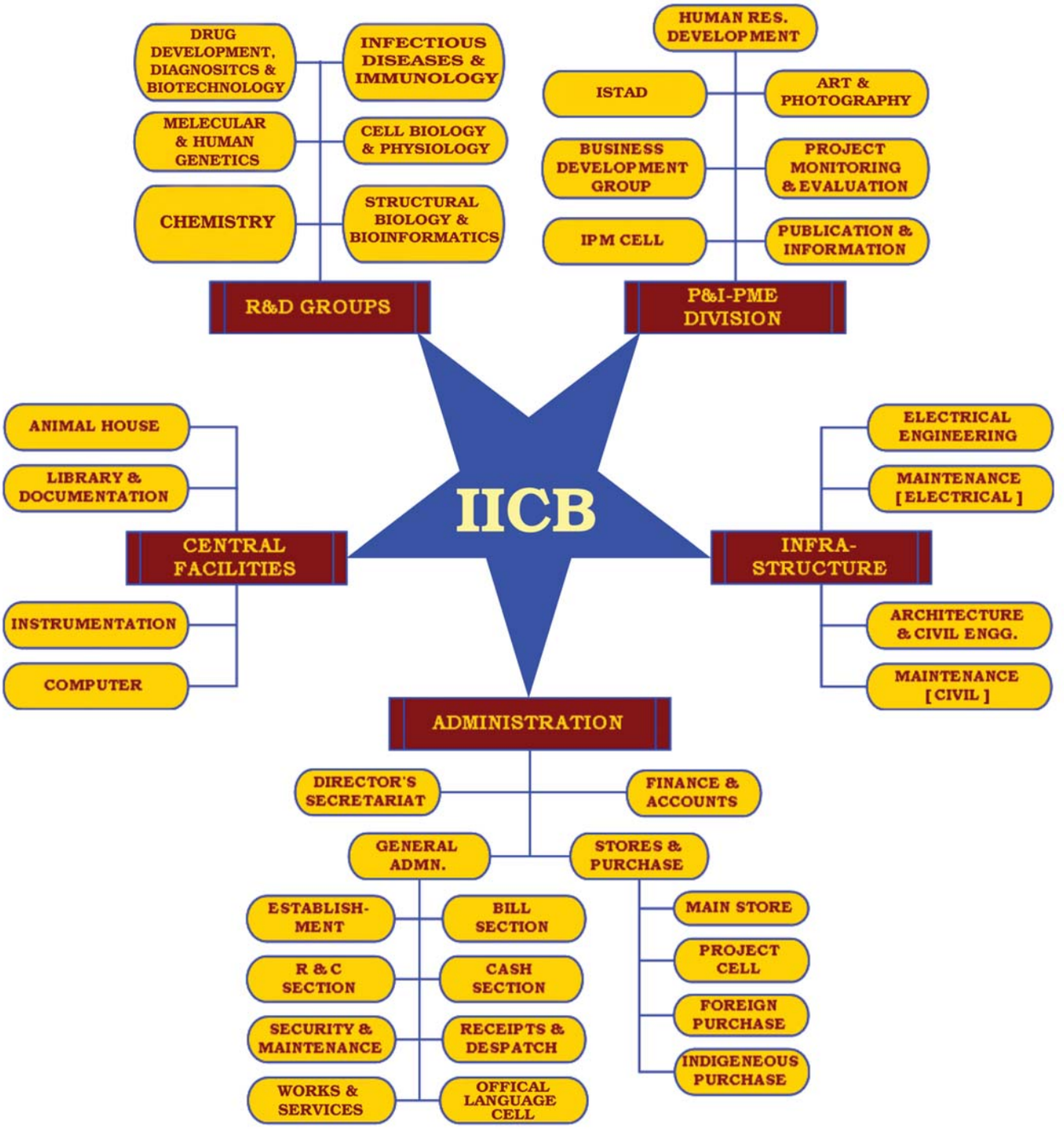
A steady number of quality publications in high to very high impact journals are the hallmark of the Institute's progress in research and the average impact factor of publications is increasing continuously. I am proud to find that the average impact factor of publications of IICB is more than 3 this year.

During the reporting period IICB has filed twenty national and international patents related to synthesis, diagnosis, extraction of bioactive compounds from herbal resources to combat kala azar, prostate cancer, blood cancer, diabetes and other common human diseases. Total nine patents, mostly in abroad, are granted for the period of 2006-07.

IICB has always remained as a choice for budding scientists with aspiration to work in biological and chemical fields. This year the institute has attracted a large number of bright, young research fellows and research associates from all over the country to generate adequate and trained human resource in the different fields of Biology and Chemistry and related areas for meeting the requirement of cutting edge research. During 2006-07 around 150 fellows and research associates worked in this Institute with strong motivation of work in basic and applied fields of research and generated excellence. A large number of distinguished scientists both from India and abroad visited, delivered lectures and hold discussions with the research groups in IICB. More than hundred students from different Universities and Institutes of India received summer training and other training programmes. A large number of Scientists were involved in teaching and training programmes of neighbouring universities and institutes. Despite organizing various scientific symposia, the institute also observed Institute Foundation day, CSIR Foundation day and celebrated 'Golden Jubilee year of IICB in CSIR' with an international symposium.

I extend my heartfelt gratitude to all the scientific, technical and administrative staff of our Institute for their year long sincere activity and cooperation in sustaining growth and maintaining the reputation of IICB. I also believe that the commitments offered by my colleagues will elevate the Institute in a new echelon in near future. Finally I must thank the Editorial Board who has done a brilliant job with their careful efforts in bringing out this report.

IICB, Kolkata **Prof. Siddhartha Roy**


IICB
R&D GROUPS
DRUG DEVELOPMENT, DIAGNOSITCS & BIOTECHNOLOGY
INFECTIOUS DISEASES & IMMUNOLOGY
MELECULAR & HUMAN GENETICS
CELL BIOLOGY & PHYSIOLOGY
CHEMISTRY
STRUCTURAL BIOLOGY & BIOINFORMATICS
P&I-PME DIVISION
HUMAN RES. DEVELOPMENT
ISTAD
ART & PHOTOGRAPHY
BUSINESS DEVELOPMENT GROUP
PROJECT MONITORING & EVALUATION
IPM CELL
PUBLICATION & INFORMATION
CENTRAL FACILITIES
ANIMAL HOUSE
LIBRARY & DOCUMENTATION
INSTRUMENTATION
COMPUTER
INFRA-STRUCTURE
ELECTRICAL ENGINEERING
MAINTENANCE [ELECTRICAL]
ARCHITECTURE & CIVIL ENGG.
MAINTENANCE [CIVIL]
ADMINISTRATION
DIRECTOR'S SECRETARIAT
FINANCE & ACCOUNTS
GENERAL ADMN.
STORES & PURCHASE
ESTABLISH-MENT
BILL SECTION
R & C SECTION
CASH SECTION
SECURITY & MAINTENANCE
RECEIPTS & DESPATCH
WORKS & SERVICES
OFFICAL LANGUAGE CELL
MAIN STORE
PROJECT CELL
FOREIGN PURCHASE
INDIGENEOUS PURCHASE

Performance at a Glance

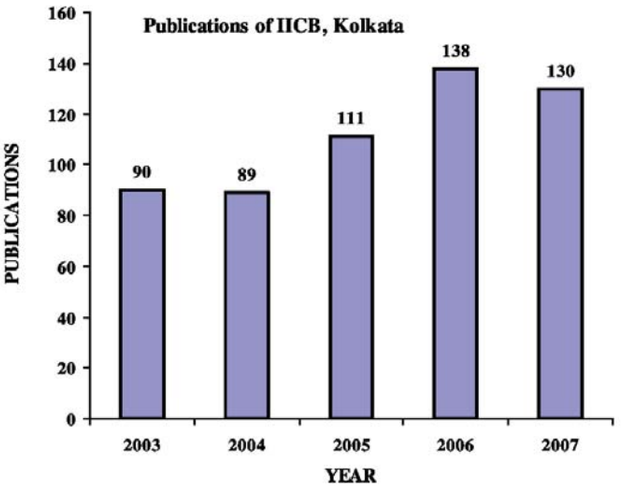
THE LAURELS

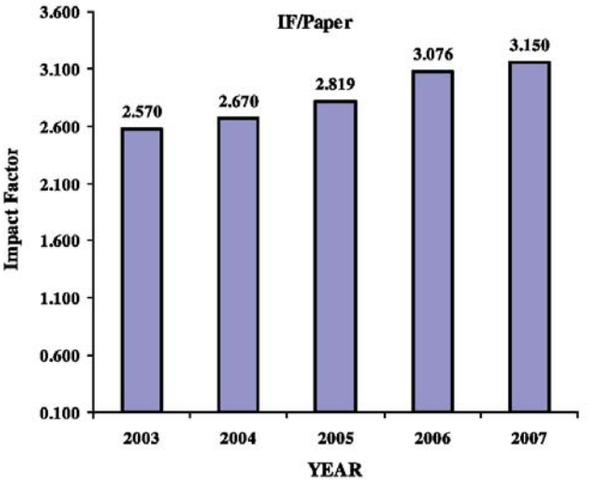
- Prof. Siddhartha Roy has been awarded "J.C. Bose Fellowship" by Ministry of Science & Technology, Govt. of India
- Dr. Pijush K. Das has been elected Fellow, Indian National Science Academy (FNA), New Delhi
- Prof. Siddhartha Roy has been elected Fellow, West Bengal Academy of Science & Technology, Kolkata
- Dr. Kunal Ray has been elected Fellow, West Bengal Academy of Science & Technology, Kolkata

Performance at a Glance

PUBLICATIONS

A steady number of quality publications are the hallmark of the Institute's progress in research. Year-wise publications* and average impact factor (IF) for the last five years are as follows:



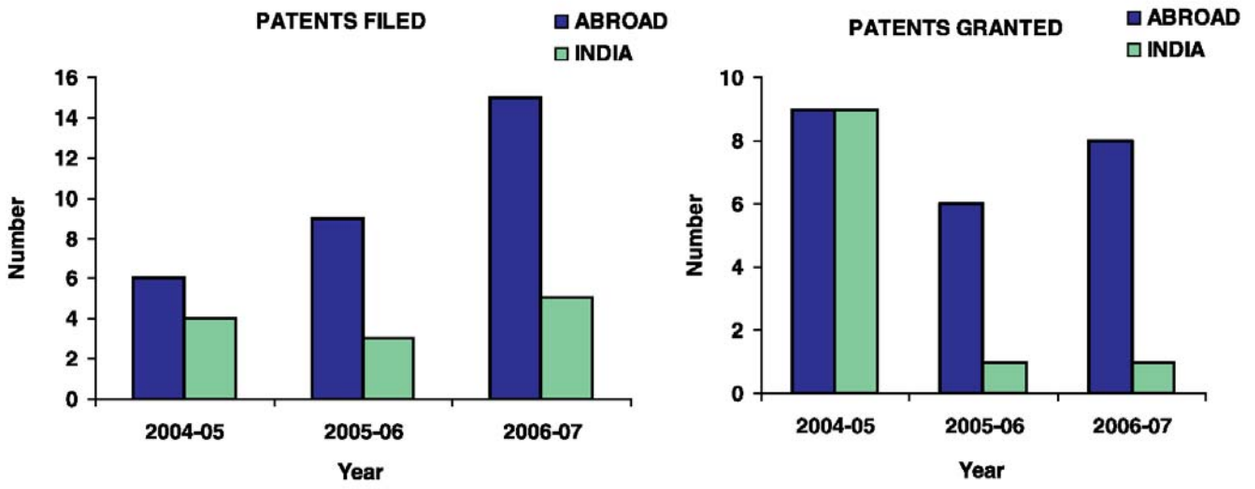


* Detailed list of publications for 2006-07 is given inside separately.

Performance at a Glance

PATENTS

A steady number of patents* are filed every year from the Institute and are granted.



* List of patents filed and granted in 2006-07 are given inside in reports of P&I-PME Division

Performance at a Glance

INDUSTRY-INSTITUTE TIE-UP

The Institute is continuously building synergy with the industries and successfully converting knowledge into wealth. This year, IICB scientists have managed to sustain the same level of interaction with the industry and earn a considerable amount of resources both human and financial.

Our partners for the overall growth towards a GATT-India regime are as follows :

- ★ Merial SAS, Lyn, France
- ★ Biotech Consortium (I) Ltd., New Delhi
- ★ Nicholas Piramal India Limited, Mumbai
- ★ Neugen Diagnostics, Secunderabad
- ★ Shantha Biotechnics Limited, Hyderabad
- ★ Evolva Biotech Private Limited, Hyderabad
- ★ Dey's Medical Stores (Mfg) Ltd., Kolkata
- ★ East India Pharmaceuticals Works Limited, Kolkata
- ★ Coir Board, Kochi;
- ★ Chembiotek Research International Pvt. Ltd., Kolkata
- ★ Zephyr Biomedicals, Goa
- ★ Qualpro Diagnostics, Goa

Performance at a Glance

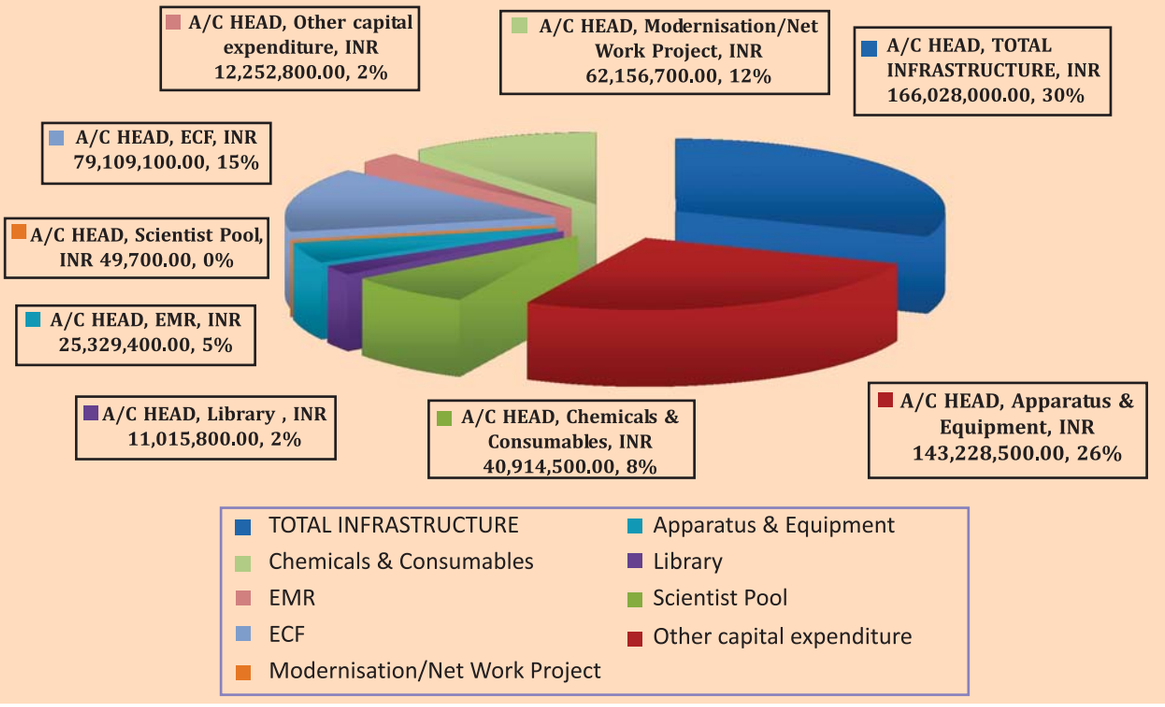
HUMAN RESOURCE DEVELOPMENT

A number of research scholars carry out research at Doctoral and Post-doctoral levels each year. Several students from various universities of the country get short-term training in every year. Data on the current year are as follows :

Number of Research Scholars	...	...	141
Number of Students received Ph.D. degrees	...	...	35
Number of Short-term Trainees	...	...	110
Number of Scientists offered lectures at various Universities/Institutes	...	...	27

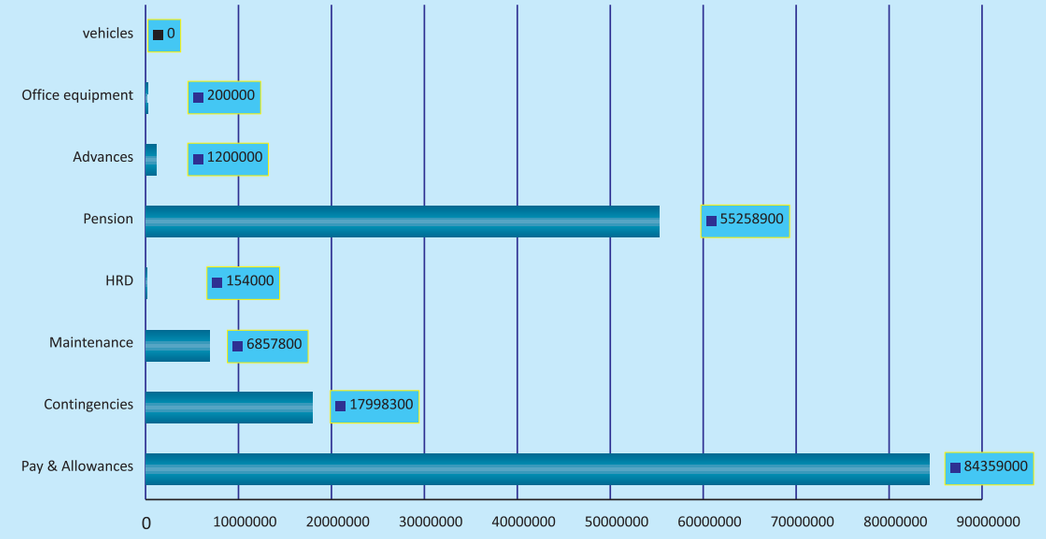
Performance at a Glance

R & D AND TOTAL EXPENDITURE BREAK-UP 2006-07



SOURCE : IICB ACCOUNTS

INFRASTRUCTURAL BREAKUP 2006-07

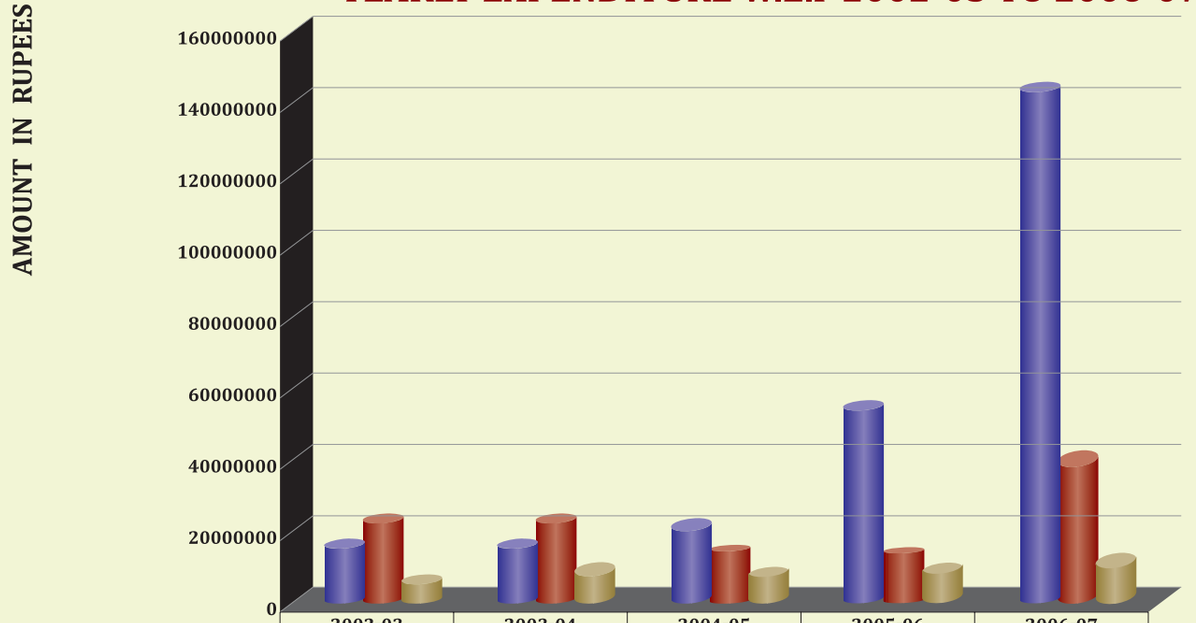


	Pay & Allowances	Contingencies	Maintenance	HRD	Pension	Advances	Office equipment	vehicles
AMOUNT IN LACS	84359000	17998300	6857800	154000	55258900	1200000	200000	0

SOURCE : IICB ACCOUNTS

Performance at a Glance

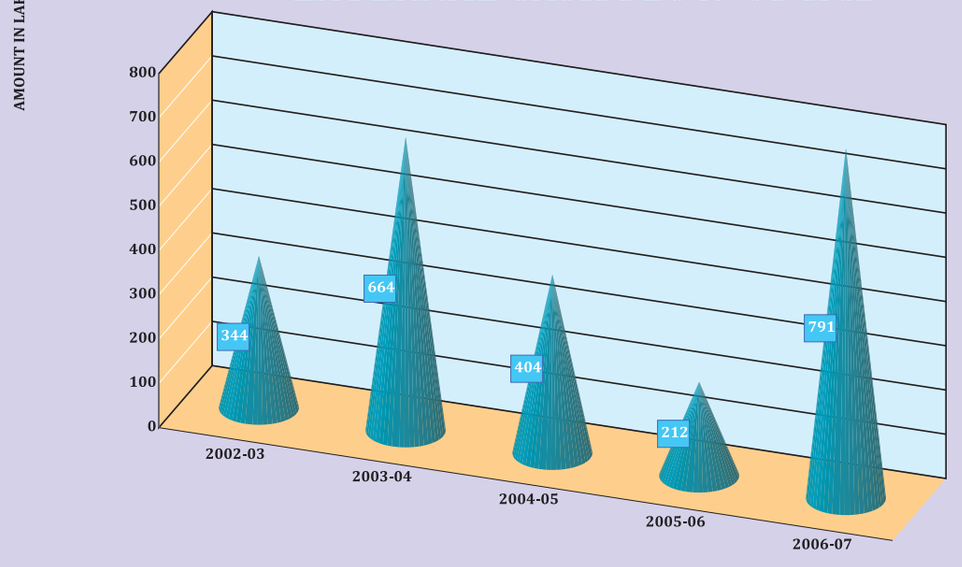
YEARLY EXPENDITURE W.E.F 2002-03 TO 2006-07



	2002-03	2003-04	2004-05	2005-06	2006-07
APPARATUS & EQUIPMENTS	15416861	6208844	21086867	53849703	143228500
CHEMICALS & CONSUMABLES	22495216	17083108	13573146	12900574	40914500
LIBRARY	5404244	8724167	7339387	8611260	11015800

SOURCE : IICB ACCOUNTS

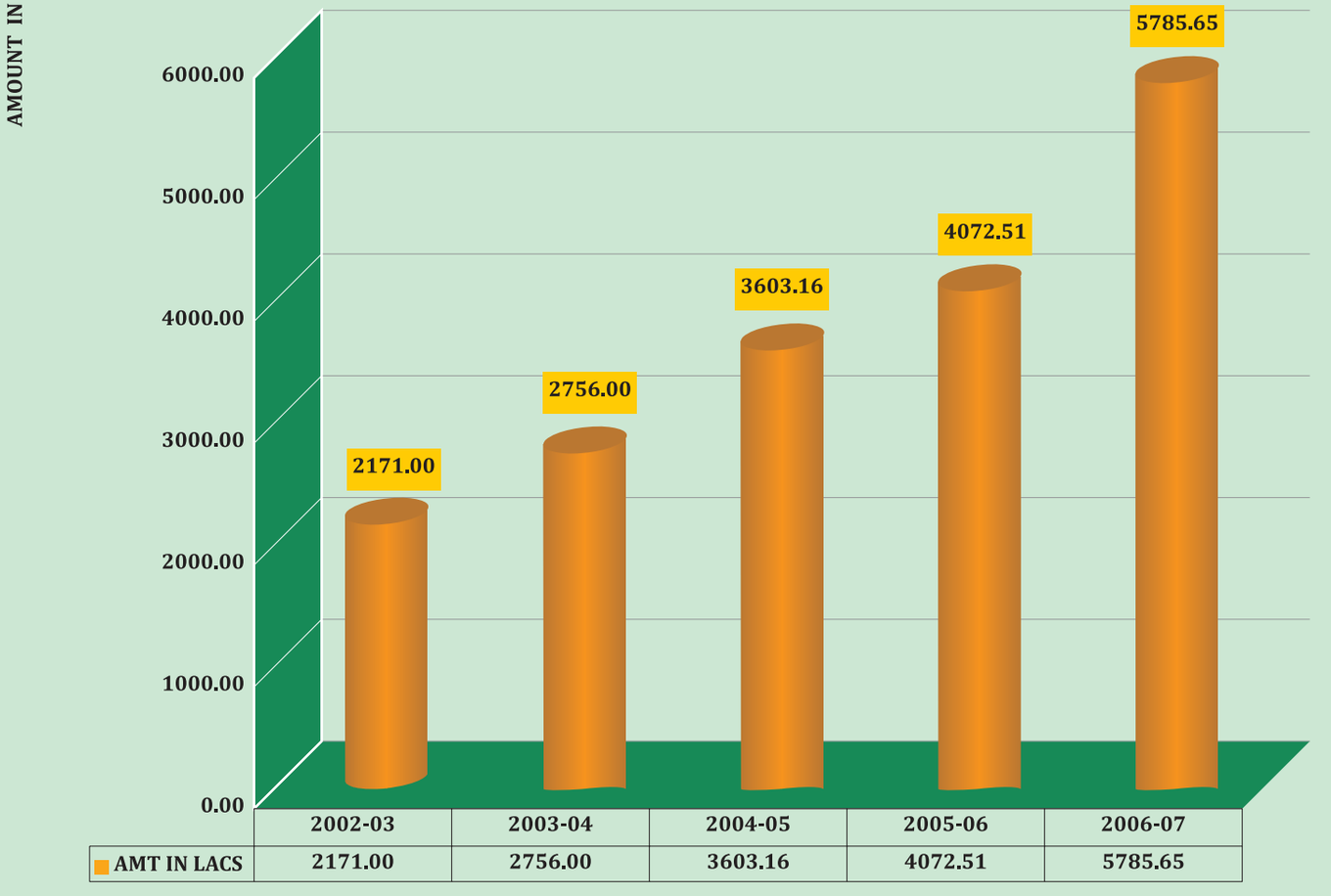
EXTERNAL CASH FLOW OF IICB



	2002-03	2003-04	2004-05	2005-06	2006-07
AMOUNT IN RUPEES	344	664	404	212	791

SOURCE : IICB ACCOUNTS

YEARWISE GRANT RECEIVED FROM CSIR



	2002-03	2003-04	2004-05	2005-06	2006-07
AMT IN LACS	2171.00	2756.00	3603.16	4072.51	5785.65

SOURCE : IICB ACCOUNTS

Infectious Diseases & Immunology

Dr. Hemanta K. Majumder, Dr. Pijush K. Das, Dr. Chitra Mandal, Dr. Syamal Roy, Dr. Santu Bandopadhyay, Dr. Nahid Ali, Dr. Rukhsana Chowdhury, Dr. Rupak K. Bhadra, Mrs. N. V. M. Khalkho, Dr. Debjani Mandal, Dr. Tripti Dey, Dr. Uday Bandopadhyay, Dr. Malini Sen, Dr. Mridula Misra, Dr. Mita Chatterjee Debnath

Research activity of infectious diseases and immunology group involves various fields of biological sciences with special interest to *Leishmania* and Cholera.

Dr. H. K. Majumder & Ms. N. V. M. Khalkho

Molecular architecture of type IB DNA topoisomerase of Leishmania

All eukaryotic topoisomerase I enzymes are monomeric enzymes, whereas the kinetoplastid family (*Trypanosoma* and *Leishmania*) possess an unusual bisubunit topoisomerase I. To determine what happens to the enzyme architecture and catalytic property if the two subunits are fused, and to explore the functional relationship between the two subunits, we describe here in vitro gene fusion of *Leishmania* bisubunit topoisomerase I into a single ORF encoding a new monomeric topoisomerase I (LdTOPIL-fus-S). It was found that LdTOPIL-fus-S is active. Gene fusion leads to a significant modulation of in vitro topoisomerase I activity compared to the wild-type heterodimeric enzyme (LdTOPILS). Interestingly, an N-terminal truncation mutant (1-210 amino acids) of the small subunit, when fused to the intact large subunit [LdTOPIL-fus-D(1-210)S], showed reduced topoisomerase I activity and camptothecin sensitivity in comparison to LdTOPIL-fus-S. Investigation of the reduction in enzyme activity indicated that the nonconserved 1-210 residues of LdTOPIS probably act as a 'pseudolinker' domain between the core and catalytic domain of the fused *Leishmania* enzyme.

The active site tyrosine residue of all monomeric type IB topoisomerases resides in the C-terminal domain of the enzyme.

The small subunit harbors the catalytic tyrosine within the SKXXY motif. To explore the functional relationship between the two subunits, we have replaced the small subunit of *L. donovani* topoisomerase I with a C-terminal fragment of human topoisomerase I (HTOP14). The purified LdTOP1L (large subunit of *L. donovani* topoisomerase I) and HTOP14 were able to reconstitute topoisomerase I activity when mixed in vitro. This unusual enzyme, 'LeishMan' topoisomerase I (Leish for *Leishmania* and Man for human) exhibits less efficiency in DNA binding and strand passage compared with LdTOP1L/S. Fusion of LdTOP1L with HTOP14 yielded a more efficient enzyme with greater affinity for DNA and faster strand passage ability. Both the chimeric enzymes are less sensitive to camptothecin than LdTOP1L/S. Restoration of topoisomerase I activity by LdTOP1L and HTOP14 suggests that the small subunit of *L. donovani* topoisomerase I is primarily required for supplying the catalytic tyrosine. Moreover, changes in the enzyme properties due to substitution of LdTOP1S with HTOP14 indicate that the small subunit contributes to subunit interaction and catalytic efficiency of the enzyme.

Topoisomerases of Leishmania with reference to development of therapeutics

The enormous development of molecular and cellular biology in recent times have provided opportunity for discovering newer molecular targets for drug designing, which form a rational basis for the development of improved anti parasitic therapy. This laboratory has been involved in developing DNA topoisomerase targeted anti-leishmanial agents.

i. The unusual, heterodimeric topoisomerse IB of *Leishmania* shows functional activity upon reconstitution of the DNA binding large subunit (LDTOPIL or L) and the catalytic small subunit (LdTOPIS or S). In this study we generated N and C-terminal truncated deletion constructs of either subunit and identified proteins LdTOPIL $^{39\text{-}456}$ (Lacking amino acids 1-39 and 457-635) and interacting region of LdTOPIL lies between residues 40-99 and 435-456, while for LdTOPIS, it lies between residues 210-215 and 245-262. The heterodimerization between the two fragments is weal and therefore co-purified fragments showed reduced DNA binding, cleavage and relaxation properties compared to the wild type enzyme. The minimal fragments could complement their respective wild type subunits inside parasites when the respective subunits were downregulated by transfection with conditional antisense constructs. Site directed mutagenisis studies identify K455 and LdTOPIL and D261 of LdTOPIS as two residues involved in subunit interaction. Taken together this study provides crucial insight into the mechanistic detail for understanding the unusual structure and inter-subunit co-operativity of this heterodimeric enzyme.

ii. We have identified 3, 3' dinodolyl methane (DIM) as potent inhibitor of *Leishmania donovani* topoisomerase I (LdTOPILS) with an IC_{50} of 1.2μM. Equilibrium dialysis experiment shows that DIM binds strongly to the free enzyme with a binding constant to 9.73 X 10^{-9} M. The binding affinity of DIM with the small subunit is 8.6 fold more than that of the large subunit of unusual bi-subunit *L. donovani* topoisomerase I. DIM stabilizes topoisomerases I-DNA cleavage complexed in vitro and also in vivo. Like camptothecin (CPT), DIM inhibits the religation step when the drug was added to pre-formed topoisomerase I-DNA binary complex. Hence, DIM is similar to CPT with respect to its ability to form the topoisomerase I-meidated "cleavable complexes" in-vitro and in-vivo. But unlike CPT, DIM interacts with both free enzyme and substrate DNA. Collectively, DIM is a noncompetitive class I inhibitor of topoisomerase I. DIM also inhibits the relaxation activity of CPT-resistant mutant enzyme LdTOP1△39LS. The IC_{50} values of DIM in simultaneous and enzyme preincubation relaxation assays are 3.6 μM and 2.9 μM respectively, which are higher than that of wild type topoisomerase I(LdTOPILS) indicating that affinity of DIM to LdTOP1△39LS is less than that of LdTOP1LS. This is the first report on DIM as an *L. donovani* toposiomerase I poison. Our study illuminates a new mode of action on enzyme inhibition by DIM that might be exploited for rational drug design in human leishmaniasis.

Apoptosis in Leishmania

Luteolin, a dietary flavone induces apoptosis like death in both promastigotes and amastigotes forms of *Leishmania*. Luteolin induces the loss of both maxicircles and minicircles which resulted in the formation of dyskinetoplatid cells. The loss of mitochondrial DNA causes reduction in the activities of mitochondial DNA causes reduction in the activities of complex I, II, III and IV of electron transport chain. The inactivation of ETC complex is associated with in mitochondrial as well as glyclolytic ATP production, which is responsible for depolarization of mitochondrial membrane potential and alteration in membrane structure. This event is followed by release of cytochrome C from mitochondria and causes an activation of caspase like protease ultimately leading to DNA degradation and cell death.

Protein kinase C (PKC) is an important constituent of the signaling pathways involved in apoptosis. We report here that like staurosporine withaferin A is a potent inhibitor of PKC. In *Leishmania donovani*, the inhibition of PKC by withaferin A causes depolarization of and generates ROS inside cell. Loss of leads to the release of cytochrome c into the cytosol and subsequently activities caspase-like proteases and oligonucleosmal DNA cleavage. Moreover, in treated cell, oxidative DNA lesions facilitate the stabilization of topoisomerase I-mediated cleavable complexes, which also contribute to DNA fragmentation. However, withaferin A and staurosporine cannot induce cleavable complex formation in vitro with recombinant topoisomerase I nor with nuclear extracts from control cells. Taken together, our results indicate that inhibition of PKC by withaferin A is a central event for the induction of apoptosis and that the stabilization of toposiomerases I-DNA complex is necessary to amplify apoptotic process.

Dr. Pijush K. Das

Macrophage biology in relation to disease pathogenesis using visceral leishmaniasis as the model macrophage disease

The work of this group is centered on studying macrophage biology using visceral leishmaniasis as a model disease of macrophage. It may be broadly divided into two aspects: direct therapeutic approaches in general for macrophage-associated diseases and indirect therapeutic approaches based on unique cellular or metabolic processes that may be exploited as drug targets. In the indirect therapeutic approaches we concentrated on two fundamental problems of parasite biology 1) the homing of *Leishmania* parasites in their physiological address and 2) mechanism by which *Leishmania* parasites neutralize the hostile microbicidal machinery of activated macrophages in order to establish infection. In our direct therapeutic approaches earlier we developed a macrophage-specific neoglycoprotein-based delivery system exploiting the exclusive presence of mannose receptors on macrophage surface. In a series of publications we demonstrated the effectiveness of this approach. However, during the course of this work we realized that parasite suppression is not the only desired criterion as far as leishmaniasis is concerned because this disease is accompanied by immunosuppression. Therefore, an ideal approach would be to use immunostimulant as an adjunct to parasite killing agent. We did lot of studies in this direction and now we are looking for compounds which can satisfy both the properties of parasite killing and lifting of immunological status. Currently we are concentrating on two molecules, cystatin, a natural cysteine protease inhibitor and 18β-glycyrrhetinic acid, a pentacyclic triterpene from Licorice root, which showed robust immunomodulatory activity as well as potent antileishmanial activity. In the current year we have studied towards generating minimal peptide sequence from cystatin having macrophage activating potential.

Resolution of visceral leishmaniasis by cystatin through NO up-regulation. Although suboptimal dose of IFN-γ was required for cystatin to induce NO production in mouse peritoneal macrophages (Fig. 1A), in in vivo situation IFN-γ was not a pre-requisite. Thus, peritoneal macrophages isolated from BALB/c mice given i.v. injection of cystatin produced significantly higher levels of NO_2((Fig. 1B). In mouse model of visceral leishmaniasis cystatin administration at a dose of 20 mg/kg/day for 4 consecutive days 10 days after infection could cause a marked

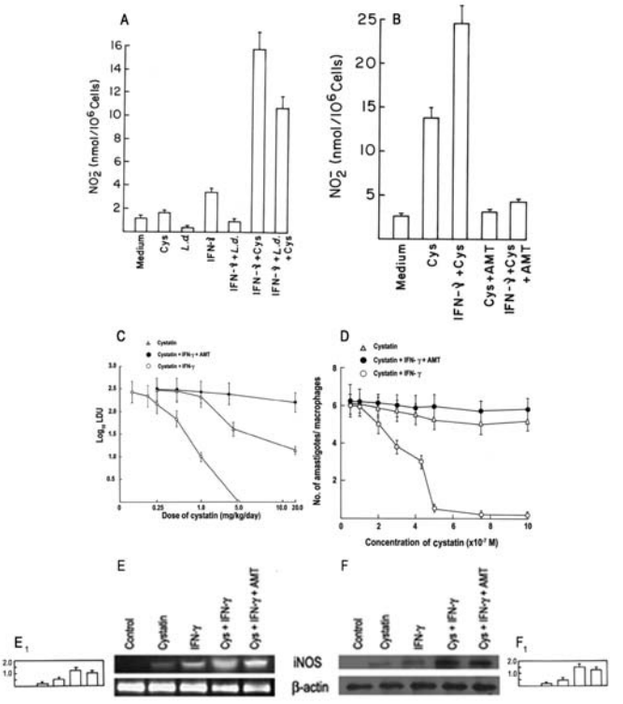


Fig. 1. Antileishmanial activity of cystatin through generation of NO. (A) NO production by peritoneal macrophages (10^6/ml) incubated for 48 h in culture medium with cystatin (5 x 10^{-7} M), *L. donovani* (macrophage:parasite ratio, 1:10), IFN-γ (100 U/ml), IFN-γ plus *L. donovani*, IFN-γ plus cystatin and IFN-γ plus cystatin plus *L. donovani.* (B) Generation of NO in peritoneal macrophages isolated from mice, which received i.v. injection of either cystatin (5 mg/kg/day) or IFN-γ (104 U/mouse) or both for 4 consecutive days. Macrophages were isolated 10 h after the last injection. Data represent the mean ± SD of three experiments. AMT (5 mg/kg/day) was used along with cystatin and IFN-γ in a separate experiment. (C) In vivo antileishmanial activity of cystatin and cystatin plus IFN-γ. Mice were challenged with 10^7 promastigotes and after 10 days of infection treated with various doses of cystatin with or without IFN-γ (104 U/mouse), i.v. daily for 4 consecutive days. Spleen parasite burden was determined 45 days after infection and is expressed as the mean $\log_{10}$ LDU ± SD of six animals. In another set of experiment, AMT (5 mg/kg/day) was used along with cystatin and IFN-γ. The $\log_{10}$ LDU of the infected control was 2.8 ± 0.08. (D) In vitro antileishmanial activity. Macrophages were infected with *L. donovani* promastigotes, excess parasites were washed off and cells were treated with graded concentrations of cystatin with or without IFN-γ (100 U/ml) for 48 h at 37°C. AMT (10 μM) was given along with cystatin plus IFN-γ in a separate set of experiment. The number of parasites inside the macrophage was counted. The infected controls had 7.22 ± 0.65 amastigotes/macrophage. The nature of iNOS was determined by RT-PCR of its mRNA transcript (E) and by Western blot analysis of its protein level (F) for various regimens. Band intensities were analyzed by densitometry (E_1 and F_1). suppression in spleen parasite burden ($\log_{10}$ LDU of 1.17 ± 0.17 compared to 2.47 ± 0.05 in untreated control; $P < 0.001$). However, when a suboptimal dose of IFN-γ (5 x 10^5 U/kg/day) was co-administered with the cystatin regime a much more pronounced effect (complete suppression of spleen parasite burden) was obtained at a much lower dose of 5 mg/kg/day of cystatin (Fig. 1C). Co-administration of 0.1 mg/kg/day of 2-amino-5,6-dihydro-6-methyl-4H-1,3-thiazine (AMT), inhibitor of inducible nitric oxide synthase (iNOS), caused reversal of the parasite suppressive effect suggesting the involvement of NO for cystatin mediated anti-leishmanial action. In the in vitro situation of amastigote multiplication within macrophages also, the inhibitory effect of cystatin in presence of 100 U/ml of IFN-γ (IC_{50} of 4.3 μg/ml) was abrogated by treatment with 10 μM of AMT (Fig. 1D). The in vivo and in vitro effect of cystatin in presence of AMT was also reflected in the iNOS mRNA expression pattern by RT-PCR and protein level by Western blot in Fig. 1E and 1F respectively. It may be mentioned that cystatin plus IFN-γ did not have any influence on the in vitro proliferation of *L. donovani* promastigotes.

Regions for NO up regulation and cysteine protease inhibition. In order to determine whether cysteine proteinase inhibitory region overlaps with the NO stimulatory region, cystatin was saturated with inactivated papain. When examined complexed cystatin was found to have comparable NO generating ability in IFN-γ activated macrophages as that of the free form (Fig. 2). Other members of the cystatin superfamily, human stefin B and T-kininogen, when complexed with reduced papain, also generated nitrite levels, which were comparable to that of the free inhibitors after 48 h of incubation, while aprotinin, an unrelated protease inhibitor, did not show any induction of NO. These results indicate the presence of a distinct NO stimulatory domain unrelated to protease inhibitory activity in cystatin and related compounds.

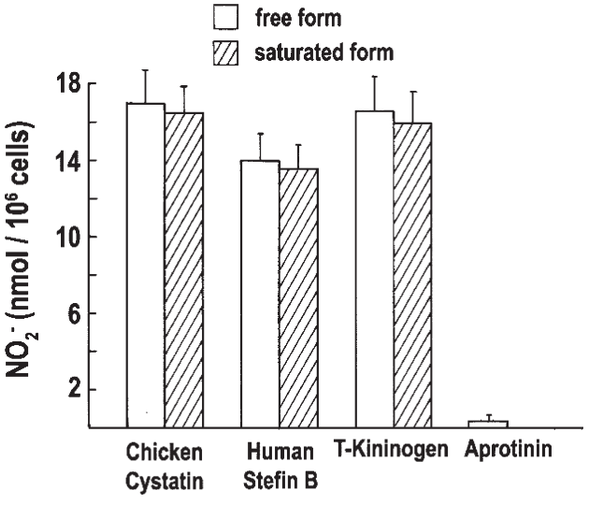


Fig. 2. Up-regulation of nitrite release by members of the cystatin superfamily, complexed with papain. Papain was inactivated by reduction and alkylation. Inactivation was checked by the complete loss of enzyme activity. The carboxymethylated papain (10^5 M) was then mixed at 37°C for 45 min with 10^6 M chicken cystatin, human stefin B or T-kininogen. The free form (open bars) or saturated forms (filled bars) were then introduced in the culture medium for 48 h before the nitrite measurement. Data represent the mean ± S.D. of three experiments.

Domain of cystatin involved in NO up-regulation. To gain insight into the region of cystatin responsible for NO up-regulation, the cDNA of cystatin was dissected into three non-overlapping fragments, designated Cst I, Cst II and Cst III, respectively, representing the NH_2-terminal region (aa residues 1-28), the intermediate region (aa residues 29-72) comprising the conserved QLSVG segment, known to play a central role in cysteine proteinase-cystatin interaction and the COOH-terminal part of the molecule (aa residues 73-116). Using sequence specific PCR primers, the respective fragments were picked up from the cDNA and ligated into a prokaryotic expression vector, which allowed the production of high amounts of the respective polypeptide as GST-fusion protein in *E. coli*. Following IPTG induction of the transformed bacteria with the respective constructs, an additional band of ~30 kD (27 kD from GST and ~3 kD from the respective non-overlapping polypeptides of cystatin) was obtained on SDS-PAGE (Fig. 3A, lanes 2, 4 and 6) whereas the lysate of induced bacteria harbouring the vector alone showed GST band of 27 kDa (Fig. 3A, lanes 1, 3, and 5). That GST fusion did not interfere with the native form of the respective polypeptides was evidenced by Western blot analysis of the fusion constructs with anti-cystatin antibody (Fig. 3B). Analysis by PAGE showed that the various recombinant

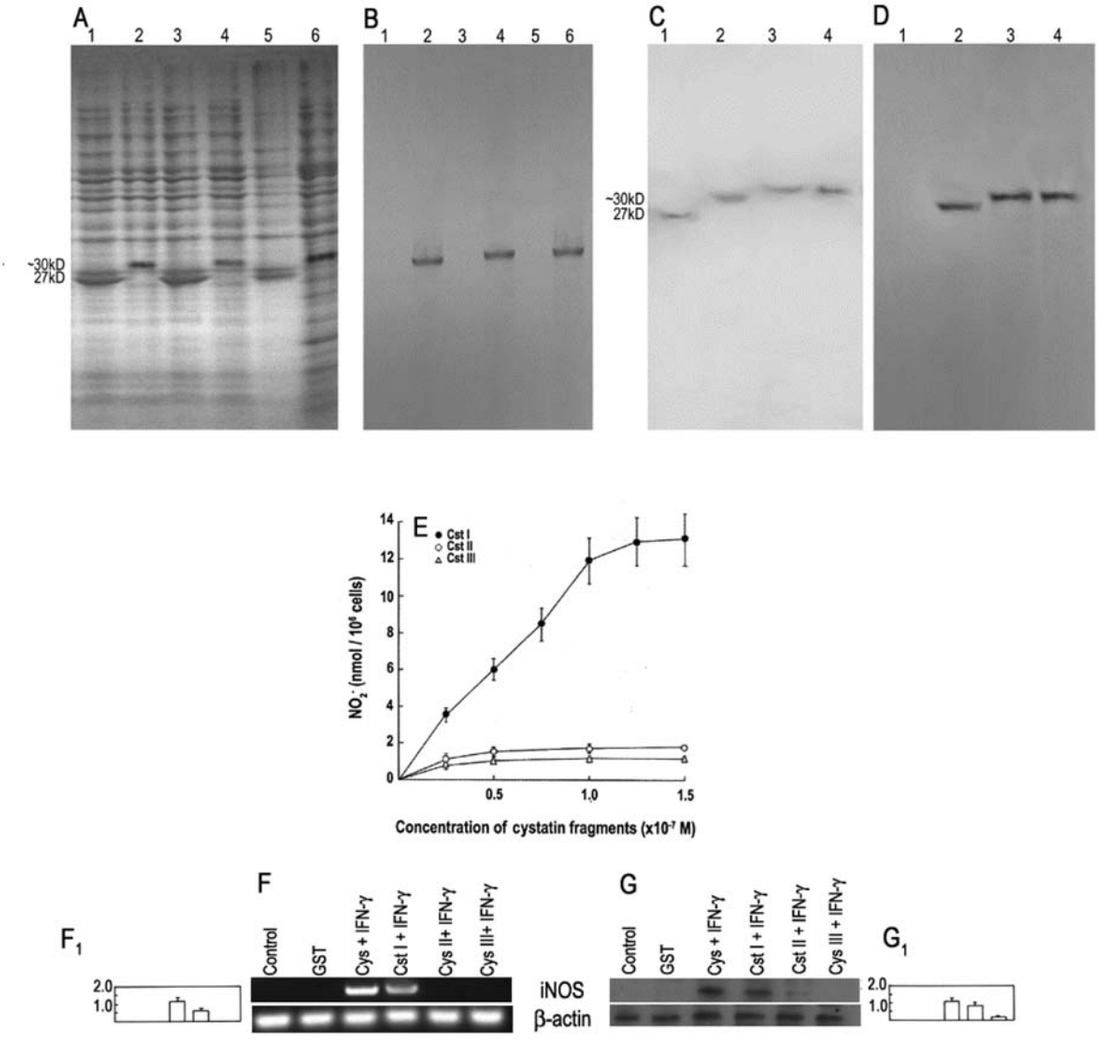


Fig. 3. Identification of the NO stimulatory domain of cystatin. (A) Three non-overlapping fragments representing the N-terminal (Cst I, 1-28 aa), the intermediate (Cst II, 29-72 aa) and the C-terminal (Cst III, 79-116 aa) domains were cloned into a prokaryotic expression vector (pGEX-5X-2) and expressed as GST-fusion protein. Lanes 2, 4 and 6 show

the coomassie stained SDS-PAGE of GST-fusion proteins (~30 kD) of Cst I, Cst II and Cst III respectively whereas lanes 1, 3 and 5 show the induced bacterial lysate. (B) The corresponding Western blot analysis using polyclonal anti-cystatin antibody. (C) The purified recombinants as GST-fusion proteins (lane 1 - recombinant GST, lane 2 - GST-Cst I, lane 3 - GST-Cst II and lane 4 - GST-Cst III) separated on 10% SDS-PAGE and (D) immunoblotted with polyclonal anti-cystatin antibody. (E) Macrophages were incubated with graded concentrations of recombinant GST-fusion products of CstI, CstII and CstIII along with suboptimal dose of IFN-γ (100 U/ml) for 48 h and the release of NO_2- was quantified. Data are mean ± SD of three experiments. The nature of iNOS expression was also determined by RT-PCR for mRNA transcript (F) and by Western blotting for protein level (G) in response to 1 10^{-7} M of cystatin and various recombinants as GST-fusion peptides along with 100 U/ml of IFN-γ. Band intensities were analysed by densitometry (F1 and G1) polypeptides purified from bacterial lysates by affinity chromatography using GST purification columns contained a single band of molecular mass of ~30 kD protein (Fig. 3C) and anti-cystatin antibody was found to react with a single band with these recombinant polypeptides (Fig. 3D, lanes 2-4). When these recombinant polypeptides were analysed for their NO generating capability, Cst I showed the maximal NO induction (12 nmol/10^6 cells at 0.1 nM concentration), while Cst II and Cst III had no significant effect (Fig. 3E). This was also reflected in the iNOS mRNA expression pattern (Fig. 3F) and protein level (Fig. 3G). When these recombinant peptides were assessed for their cysteine protease inhibitory activity with papain, only the intermediate fragment Cst II inhibited papain with a Ki of 900 nM. Both Cst I and Cst III exhibited > 1000-fold weak inhibition as compared to the whole molecule indicating thereby that the N-terminal region of cystatin is not involved in cysteine protease inhibition, but has a role to play in NO up-regulation.

Cystatin-derived immunomodulatory peptide exhibiting leishmanicidal activity. To determine whether the NO generating capability of the N-terminal domain of cystatin could be narrowed down to a minimal aa sequence, a set of 6 synthetic overlapping peptides (compounds 1-6) of 8 amino acids each, spanning the entire 28 aa of Cst I were assessed. Maximum NO generating ability was found to be associated with compound 4 (Fig. 4A). Further, using 4 overlapping peptides of 10 aa (compound A-D) covering the 8 amino acids of compound 4, a 10-mer region (compound B) from position 11-20 of Cst I was found to be the domain responsible for NO stimulatory activity (Fig. 4B) which is comparable to that of the whole cystatin molecule. NO_2- release by macrophages progressively increased with increasing concentration of compound B until 1 μM, when it reached a maximum level (Fig. 4C). In order to ascertain the specificity of this compound, a rabbit polyclonal antibody was raised against this 10-mer region. The presence of 5 μg/ml of the anti-peptide antibody could almost totally abrogate the NO generation at concentrations as high as 5 μM of compound B (Fig. 4C). We then examined the efficacy of compound B on intracellular growth of amastigotes within macrophages. *L. donovani*-infected cultures were treated with graded concentrations of compound B, ranging from 0.1 to 5 μM, in the presence of sub-threshold concentrations of IFN-γ. As shown in Fig. 4D, compound B exhibited profound antileishmanial activity with an IC_{50} of 0.52 μg/ml. Both AMT, a specific iNOS inhibitor and anti-peptide antibody.

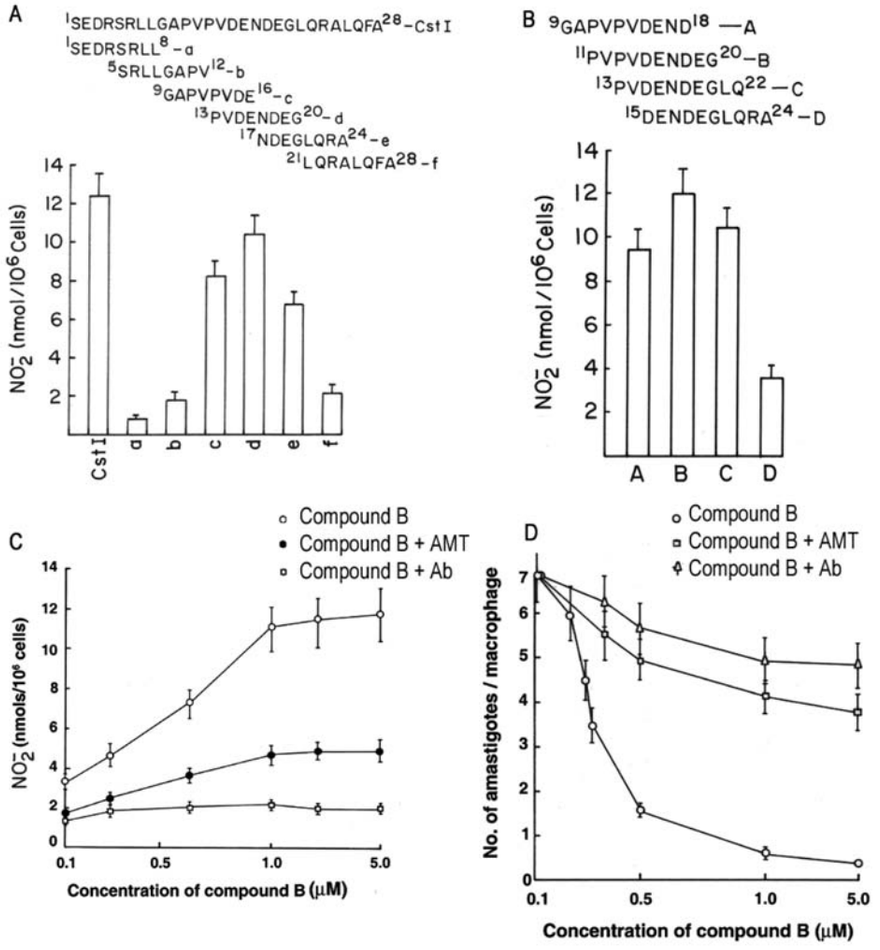


Fig. 4. Minimal peptide sequence with NO stimulatory potential and its antileishmanial activity. (A) Macrophages were incubated with overlapping synthetic peptides (8-mer) derived from CstI along with IFN-γ (100 U/ ml) and NO2- release was quantified. (B) NO_2- release from macrophages was measured in response to overlapping 10-mer peptides containing most potent 8-mer peptide in terms of NO production. (C) Dose-response curves of various concentrations of compound B in combination with IFN-γ (100 U/ ml) for the release of NO_2- by macrophages in the presence or absence of either anti-compound B antibody or AMT (10 μM). (D) Infected macrophages were treated with graded concentrations of compound B in combination with IFN-γ (100 U/ml), in the presence or absence of either anti-compound B antibody or AMT (10 μM). Infected controls contained 7.14 ± 0.69 amastigotes/macrophages. Data are mean ± SD of three experiments. could cause a reversal of antileishmanial effect suggesting thereby that the antileishmanial effect of compound B may be correlated to increased production of NO.

Effect of cystain-derived 10-mer peptide in experimental leishmaniasis. The efficacy of 10-mer peptide for the treatment of visceral leishmaniasis in vivo was determined with a mouse model. BALB/c mice were infected i.v. with *L. donovani* AG83. Animals were given i.v. infections of graded dose (0.01 to 1.0 mg/kg/day) of peptide along with a constant dose of 10^4 U of IFN-γ daily for 4 consecutive days 10 days after infection and infection was allowed to proceed for 45 days. The degree of leishmanicidal potency of the peptide was assessed in terms of liver and spleen parasite burden. 93% and 95% reduction in liver and spleen parasite burden respectively was obtained at a dose of 0.5 mg/kg/day (Fig. 5A). In the placebo treated infected controls a high burden of parasites were present in liver ($\log_{10}$ LDU of 3.41 ± 0.32) and spleen ($\log_{10}$ LDU of 2.32 ± 0.21). This was also the case in animals receiving anti-peptide antibody in conjunction with compound B treatment.

Reinfection of cured animals after 45 days resulted in only a slight and transient increase in organ parasite burden suggesting possible development of protective immunity (Fig. 5B). To ascertain whether compound B-treated mice also control the infection by a NO-dependent mechanism, AMT (5 mg/kg/day) was administered one week after reinfection. Within 3-4 days of AMT administration the organ parasite burden started increasing. The infection was under control again after AMT was withdrawn (Fig. 5B).

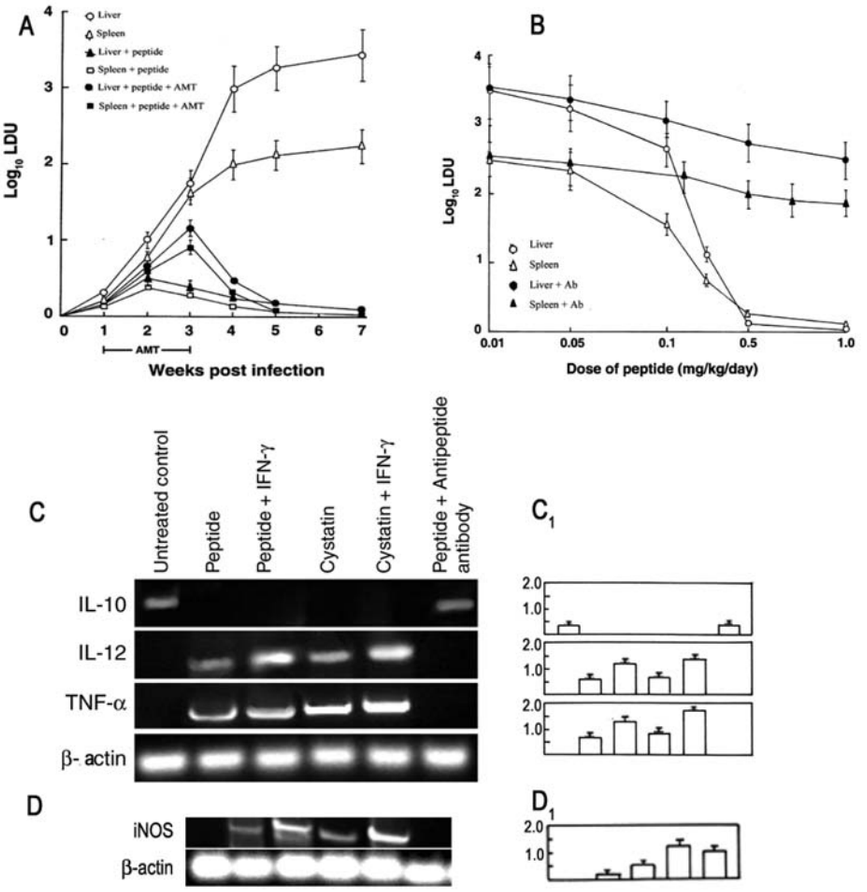


Fig. 5. Effect of compound B treatment on visceral infection in BALB/c mice. (A) Various doses of compound B ranging from 0.05 to 1 mg/kg/day were given i.v. along with IFN-γ (10^4 U/mouse) for 4 consecutive days 10 days after infection. The parasite burdens in liver and spleen were then determined at 45 days after infection. Anti-peptide antibody was given along with compound compound B and IFN-γ in a separate set of experiment. (B) The course of visceral reinfection was studied by i.v. administration of 10^7 promastigotes into naïve, age-matched BALB/c mice and cured (1mg/kg/day compound B-treated) mice. In one group of cured mice, AMT (5mg/kg/day) was i.v. administered 1 wk after reinfection for 2 wk. Determining liver and spleen parasite burdens, expressed as Log_{10}LDU, monitored the progression of infection in all the cases. Results are from three experiments and indicate the mean ± SD for 5 to 7 mice at each time point. (C) Cytokine profile in *L. donovani-infected* mice as analysed by RT-PCR. Expression of IL-10, IL-12, TNF-α, iNOS and β-Actin mRNA by spleen cells of infected mice treated i.v. with either peptide and/or IFN-γ in the presence or absence of antipeptide antibody, and compared to cystatin and IFN-γ treatment. RT products were visualized by ethidium bromide staining. RNA samples were obtained from five mice in each group. Results are representatives of five separate samples. β-Actin expression levels were used as controls for RNA content and integrity.

Effect of cystatin on cytokine production. To gain an insight into the type of immunological response in *L. donovani* infected mice after peptide therapy, mRNA transcription levels for IL-10, IL-12p40 and TNF-α were determined on isolated splenocytes 45 days after infection. There was a high level of IL-10 in infected untreated controls and a low expression level of transcripts for IL-12 and TNF-α (Fig. 5C). On the contrary, a high level of IL-12 and TNF-α expression and a very low level of IL-10 expression were detected in infected cystatin treated as well as cystatin plus IFN-γ treated cases (Fig. 5C). Inducible NOS was also found to be up-regulated in infected cystatin-treated and cystatin plus IFN-γ-treated cells (Fig. 5D). Transcript levels of various cytokines and iNOS after peptide as well as peptide plus IFN-γ therapy were found to be comparable with infected cystatin-treated and cystatin plus IFN-γ treated cells respectively (Fig. 5C and D). To determine the specificity of peptide therapy, we applied 500 µg of anti-peptide antibody along with peptide plus IFN-γ to *L. donovani*-infected mice. The anti-peptide antibodies greatly reduced peptide-mediated splenocyte iNOS as well as Th1 cytokine induction at mRNA level (Fig. 5C and D). The therapeutic effect of 10-mer cystatin-derived peptide may be attributed to the up-regulation of iNOS resulting from the up-regulation of Th1 cytokines.

Future plans include (i) detailed molecular characterization of a comprehensive cyclic nucleotide signaling in the infectivity of Leishmania parasites, (ii) in vivo effects of GRA regarding organ specificity, pharmacokinetics as well as various upstream signaling pathways for NF-(B activation leading to up-regulation of iNOS and Th1 cytokines and (iii) signal transduction mechanisms leading to the immunomodulatory activity of cyststin.

Dr. Chitra Mandal

Impact of glycosylation of biomoleculs in health and disease

The expanding field of glycobiology deals with the investigation of carbohydrate molecules and the role they play in biological systems. Carbohydrates specially sialic acids and its derivatives are emerging as important determinants of the immune response which is reflected in its regulation of a multitude of cellular and molecular interactions ranging from cell-cell adhesion, signaling, differentiation and metastasis. The main attention of this laboratory is focused on the understanding of the importance of glycosylation in different diseases. The identification of modified carbohydrate structures and its utility as potential disease specific biomarkers for monitoring the disease status for the following projects.

Status of disease specific sugar molecules in Indian Visceral Leishmaniasis (VL) and their clinical applications

The main outcome of the present study is to identify the molecular markers for development of a user friendly, simple blood based assay for the diagnosis of VL by detecting disease specific antigen and successfully transferred this technology to Zyphyr Biomedical, Goa.

We have earlier conclusively established that an enhanced presence of 9-O-acetylated sialoglycoconjugate (9-O-AcSG) triggers the alternate complement pathway in Indian VL. Antibodies directed against these glycotope able to activate the classical complement pathway. Several complement activators (Anti-O-AcSG antibodies; IgG, IgM, total) were affinity purified from both normal and patients' sera. Complement activation via classical pathways elicited deposition of C3 as early as 3 minutes that triggered parasite lysis. Accordingly, we have concluded that anti-O-AcSGs antibodies are important source of classical complement activator even under normal physiological conditions suggesting their role in conferring host protection against parasite infection.
Future Plan :

* Immunomodulatory role of these newly identified molecules (9-O-AcSGs)
* Investigation of differential glycosylation pattern on different clinical isolates
* Biological significance of differentially expressed sialoglycans proteomic of a few affinity purified sialoglycans from VL patients and parasites

Study of O - acetylated sialoglycoconjugates (Neu5,9Ac2-GPsALL) in childhood Acute Lymphoblastic Leukemia (ALL), their immunological role and clinical applications

Earlier studies have demonstrated an over expression of Neu5,9Ac2-GPsALL on lymphoblasts and erythrocytes in children with ALL. Three distinct leukaemia-specific molecular determinants were affinity purified. The enhanced presence of anti-Neu5,9Ac2-GPALL antibody has been explored to develop an Antigen-ELISA using purified Neu5,9Ac2-GPsALL as coating antigens. This study demonstrated the potential of purified Neu5,9Ac2-GPsALL in diagnosis and monitoring of these children. Additionally, newly identified circulatory immune-complexed Neu5,9Ac2-GPALL has also been explored for disease management. The role of Neu5,9Ac2-GPsALL in the survival of lymphoblasts has been observed.

We have demonstrated high induction of anti-Neu5,9Ac2-GPsALL antibodies towards the glycotope having terminal 9-O-acetylated sialic acid linked sub terminal N-acetyl galactosamine in (2-6 linkages (9-OAcSA(2-6GalNAc), at disease presentation which contribute toward immune-surveillance. Affinity purified anti-Neu5,9Ac2-GPsALL revealed a predominance of IgG2 differing in content and nature of glycosylation with normal controls. Anti-Neu5,9Ac2-GPsALLIgG2 was unable to trigger activation of Fc?R, the complement cascade, cell mediated cytotoxicity, along with impairment of a few Fc-glycosylation-sensitive effector functions hinting towards a disbalanced homeostasis thereby evading the host defense, although its glycotope binding ability remains unaffected.

Future plan:

Following aspects will be explored

* Production of chimeric antibodies for therapeutic applications.
* Glycolipid profile of lymphoblasts and their biological role in patients
* Identification and characterization of several enzymes responsible for O-acetylation of sialic acids specifically induced on lymphoblasts
* Proteomic of a few affinity purified sialoglycans from lymphoblasts of these children
* Search for new antileukemic compound
* Factors responsible for mobilization of hematopoietic stem cells in ALL

Studies on hematopoietic stem cell and its potential application in biomedical (CMM002)

The main objectives of the proposed project are to identify and characterize normal population stem cells from bone marrow (BM) as well as peripheral blood (PB) from children with leukemia for their potential application. Accordingly, different derivatives of sialic acids on stem cells were evaluated at presentation of the disease. A distinct pattern of differential sialylation among BM and PB stem cells has emerged out. The putative role of these sialic acid derivatives in mobilization and maturation will be explored.

Investigation of human C-reactive protein in various acute phase responses

C-reactive protein (CRP) is a clinically important acute phase protein whose level increases upto 1000 folds in acute inflammatory conditions. We have demonstrated, for the first time, that human CRP is glycosylated and existence of disease-specific molecular variants. Although, phosphorylcholine (PC) is a classical ligand for CRP, we have recently reported a Staphylococcus aureus cell-surface Protein A as a new ligand establishing an extended definition of CRP.

Future plan: Binding of these CRPs to microbes and parasites and their biological implication are in progress.

Dr. Syamal Roy

Antigen presentation in experimental visceral leishmaniasis

The disease visceral leishmaniasis is characterized by the depression of the cell mediated immunity (CMI) the cause of which is still unknown. The parasites replicate with in macrophage of the mammalian hosts. The infected macrophages show increase in membrane fluidity which could be corrected by the liposomal delivery of cholesterol. The increase in fluidity in macrophage is associated with defective T-cell stimulating ability and this could be corrected by the liposomal delivery of cholesterol in infected macrophage. This observation prompted us to look into therapeutic efficacy of liposomal delivery of cholesterol in infected hamster model. Our study showed that single injection of liposomal delivery of cholesterol in late stage infected hamster offered significant level of protection as evident from the reduction in the splenic and hepatic parasite burden. This allowed us to window number of cholesterol mediated cellular phenomena associated with protection. This therefore promises to be another area of disease mechanism and treatment.

Immunotherapy against experimental visceral leishmaniasis

Implementing hybrid cell vaccination (HCV) approach in infectious disease model for the first time, dominant *Leishmania* antigen-KMP-11 transfected syngeneic bone-marrow derived Mϕ (BMDM) from BALB/c mice (H-2^d) electrofused with allogeneic bone-marrow derived DC (BMDC) from C57BL/6 (H-2^b) was used to treat late stage *L. donovani* infection in susceptible BALB/c mice. HCV treatment completely cleared splenic and hepatic parasite burden resulting in high KMP-11 specific MHC class I restricted $CD8^+$CTL response along with substantial increase of both antigen-specific IFN-γ producing $CD8^+$ T cells and IL-4 producing $CD4^+$T cells. Moreover splenic lymphocytes of cured animals not only showed enhancement of prototype Th1 cytokine IFN-γ but also significant upregulation of the Th2 locus cytokines-IL-4, IL-5 and IL-13 both at transcriptional and translational levels. Similar therapy with KMP-11 transfected syngeneic BMDM and BMDC only partially reduced organ parasite load with weaker CTL response and high IFN-γ but lower Th2 locus cytokines expression compared to cured mice. Although splenic $CD4^+$ T cells from HCV treated mice when coincubated with promastigotes showed upregulation of T-bet but Gata-3 transcription factor expression was also substantially increased. $CD8^+$ T cell depletion not only reversed HCV mediated curative immunity but also resulted in a regulatory effect on $CD4^+$T with further downregulation of Th2 locus cytokine genes and Gata-3 despite extremely high IL-10 production. Our study shows that $CD8^+$T cells exert contra-suppressive effect on the coordinately regulated Th2 locus cytokines but not IL-10 due to HCV mediated curative immunotherapy and therefore might be optimally required for vaccine induced anti-leishmanial immunity.

Understanding the role of host ABC transporter in antimony resistance in experimental leishmaniasis and kala azar

Infection with Sb-resistant Leishmania donovani (SbR-LD) unlike that with Sb-sensitive (SbS-LD) not only induces elevation of GSH levels but also up regulation of multi-drug resistance-associated protein-1 (MRP1) and permeability glycoprotein (P-gp) in both in vitro and in vivo experimental infections. This results in clearance of Sb from the infected cells following sodium antimony gluconate (SAG) treatment and favors parasite replication. Inhibition of MRP1 and P-gp with resistance modifying agents (RMA) such as lovastatin allows Sb accumulation and parasite killing within macrophages and offers protection in an animal model in which infection with SbR-LD strains is otherwise constantly lethal. The occurrence of a similar scenario in clinical cases is supported by the findings that monocytes from SAG unresponsive kala-azar (KA) patients not only have elevated GSH levels but also overexpress P-gp and MRP1 as compared to monocytes from SAG sensitive KA patients. These observations usher in a new strategy for treatment of Sb resistant KA patients.

Dr. Santu Bandopadhyay

Regulation of anti-cancer activity of curcumin with reactive nitrogen species scavenger

Curcumin is a potential anti-cancer agent. A number of clinical trials are in progress with curcumin. Literature search suggests that curcumin's anti-cancer activity is attributed to inhibition of NF-κB, generation of superoxide etc. In the present study, we evaluated the effect of antioxidants on anti-cancer acitivity of curcumin. In addition we studied additional mode of actions of curcumin. We showed, for the first time, that curcumin-induced nitric oxide (NO) plays a key role in the cell death. Curcumin-induced death of chronic myeloid leukemic cell line K562 is virtually completely reversed by scavenging NO with a specific NO scavenger, carboxy-PTIO. Attempts to identify the source of curcumin-induced NO rules out the role of eNOS, nNOS or iNOS. These data suggest that mitochondrial NOS may play a key role in curcumin-induced NO which makes the lethal hit. Experiments are in progress to validate this possibility.

Dr. Nahid Ali

Leishmanial antigens in prevention and treatment of visceral leishmaniasis

Visceral leishmaniasis (VL) is a life threatening disease characterized by uncontrolled parasitization of the liver, spleen and bone marrow. There are 500,000 new cases of VL annually with ninety percent occurring in the Indian subcontinent, Sudan and Brazil. However, there are no vaccines against any form of leishmaniasis in routine clinical use. Leishmanization till date is the only proven vaccine in human beings for cutaneous leishmaniasis, but is now discontinued due to unacceptable occurrence of lesions. Although crude antigen vaccine approaches are not ideal, they indicate that protection against leishmaniasis is feasible. Extensive experimental studies against cutaneous leishmaniasis have led to the identification of promising defined protein vaccine candidates. In comparison, few antigens have been identified against the visceral disease. In our laboratory we found that soluble leishmanial antigens (SLA) extracted from *Leishmania donovani* promastigote ghost membrane are themselves immunogenic and could induce partial protection against VL. Immunization with these antigens in differently charged liposomes showed almost complete protection in association with cationic liposomes. Production of both IFN-γ and IL-4 with a dominance of Th1 response following immunization was required for optimum success against L. donovani infection in BALB/c mice. The best vaccine formulation, SLA in positively charged liposomes, was then used for immunotherapy. This vaccine induced more than 90% elimination of parasites from both liver and spleen. The success of immunotherapy exhibited an immune modulation with surge in Th1 cytokines, IFN-γ and IL-12 with extreme down regulation of Th2 cytokines, IL-4 and IL-10. These findings suggest that an immune modulation towards Th1 is effective for both successful vaccination and immunotherapy.

Therapeutic efficacy of stearylamine-bearing cationic liposomes against L. donovani infection

Despite extending treatment regimens, parenteral administration and toxic effects, the pentavalent antimonial sodium antimony gluconate (SAG) has remained the first line treatment for kala-azar. However, frequent therapeutic failures and emergence of resistance to SAG necessitate the use of second line drugs such as amphotericin B, pentamidine and miltefosine. These drugs, however, are limited in use due to their toxic effects. Liposomal drug carriers are ideal for the treatment of VL. They not only protect the host from the toxicities of the drug but also target them to the cells (macrophages) which harbor the parasites. Earlier we reported on the anti-leishmanial efficacy of drug-free liposome vesicles composed of phosphatidylcholine (PC) and stearylamine (SA). We are now formulating drugs such as SAG, amphotericin B, etc., in these vesicles to improve the therapeutic potency of the drugs through synergistic activity of PC-SA. Drugs thus formulated demonstrated almost complete clearance of parasites from liver as well as spleen and bone marrow, organs which harbor persistent parasites, through a single-shot treatment with minimal drug dosages. The mode of

action of the vesicles, and involvement of possible immunological mechanisms supporting the chemotherapy are under investigation.

Drug-induced differential polarization of the immune response in Indian kala-azar patients

The disease kala-azar is characterized by strong antibody production and suppressed cellular immunity during pathogenesis, while restoration of CMI and life-long immunity marks effective cure after chemotherapy. The drug induced immune modulation through treatment with SAG, and amphotericin B for SAG-unresponsive patients, necessitates investigation to understand the mechanism of drug-resistance, and could also be relevant to our understanding of the development of PKDL. Effective host defense requires the induction of IFNγ and IL-12, cytokines that are elicited by both SAG and amphotericin B. A differential decline of IL-10 and TGFβ were observed through therapy with these two drugs with persistence of residual IL-10 and TGFβ in SAG treated patients versus absence of IL-10 and negligible TGFß through treatment with AmB. The significane of these observations are being investigated in the contest of the development of PKDL in India.

Dr. Rukhsana Chowdhury

Bile and unsaturated fatty acids are GM1 receptor antagonists of cholera toxin and Escherichia coli heat-labile enterotoxin

We have previously demonstrated that bile and unsaturated fatty acids exert important effects on the expression of virulence factors and motility of *Vibrio cholerae*. We have now identified another effect of unsaturated fatty acids on cholera toxin, the major virulence factor of *V. cholerae*.

Cholera toxin (CT) is an archetypal bacterial toxin that binds with high affinity to the receptor ganglioside GM1 on the intestinal epithelial surface and causes the severe watery diarrhea characteristic of the disease cholera. Blocking the interaction of CT with receptor GM1 is an attractive approach for therapeutic intervention. We have demonstrated that bile prevents interaction of CT with GM1. The unsaturated fatty acids detected in bile, arachidonic, linoleic, and oleic acids, were found to be most effective. Bile and the unsaturated fatty acids interacted with CT and not GM1 to prevent CT-GM1 binding. The Kd of CT-lonoleic acid binding was calculated to be 0.13 mM. Using the rabbit ileal loop model it was demonstrated that practically no fluid accumulated in the intestinal loops when CT was administered together with inhibitory concentrations of linoleic acid. Bile and unsaturated fatty acids also inhibited the binding of *Escherichia coli* LT toxin to GM1 and no fluid accumulation was observed in rabbit ileal loops when LT was administered together with linoleic acid. These results suggest the possibility that oral administration of unsaturated fatty acids, preferably together with ORS, could be used as a precautionary and therapeutic measure for cholera and possibly travellers' diarrhea. Unsaturated fatty acids abundantly present in our daily diets, are not toxic to humans, indeed linoleic acid is an essential fatty acid, thus they might be used as drugs without fear of toxic side effects. Moreover, since they act on secreted toxins and not on the bacteria, the possibility of bacterial resistance does not arise. Further studies on cholera patients are necessary to confirm the efficacy of unsaturated fatty acids in the treatment of cholera.

Global effects of cytosine methylation on gene expression in V. cholerae

Cytosine methylation is a common epigenetic modification in prokaryotic and eukaryotic genomes. In eukaryotes, cytosine methylation is associated with a repressed chromatin state and transcriptional silencing and has a role in important biological processes like aging and development, and diseases like cancer and schizophrenia. In prokaryotes however, the only known function of methyl-cytosine is in the context of restriction-modification. We have previously characterized an 'orphan' cytosine methyltransferase in *V. cholerae*. We have now demonstrated that cytosine methylation has global effects on gene expression in the bacterium *Vibrio cholerae* and affects stress survival, motility and virulence of this important human pathogen. Cytosine methylation had

little effect on transcription initiation but reduced the efficiency of transcript elongation by RNA polymerase over the methylated regions.

Dr. Rupak K. Bhadra

Genetic organization of pre-CTX and CTX prophages in the genome of an environmental Vibrio cholerae non-O1, non-O139 strain

The cholera toxin (CT) is an important determinant of the virulence of epidemic *Vibrio cholerae* strains. The *ctxAB* operon coding for CT is part of the genome of a filamentous bacteriophage CTXϕ, which may integrate as a single or as multiple copies in the genome of *V. cholerae*. The CTXϕ genome is comprised of RS2 (2.4 kb) and core (4.5 kb) regions. Extensive genetic mapping analyses of the genome of an environmental *V. cholerae* strain VCE232 belonging to serogroup O4 indicated presence of two copies of tandemly arrayed CTX prophages integrated in the small chromosome (Fig. 6). Further mapping revealed that the integration of prophages has occurred in the same genetic locus of the small chromosome of VCE232 as it was found in V. cholerae O1 biotype El Tor strains. Interestingly, a new type of RS2-like element of 3.5 kb in size was found in the CTX prophage genome in the small chromosome of VCE232 (Fig. 6). Cloning followed by sequencing of the new RS2-like element of VCE232 revealed presence of three ORFs, which probably codes for highly divergent types of phage regulatory proteins. Furthermore, the strain VCE232 also harbors two copies of tandemly arranged CTX prophage devoid of the *ctxAB* genes, called pre-CTX prophage, in its large chromosome. The presence of multiple copies of diverse CTX prophages in both the chromosomes of VCE232 suggest that toxigenic environmental *V. cholerae* non-O1, non-O139 strains could play a role in the emergence of new epidemic clones.

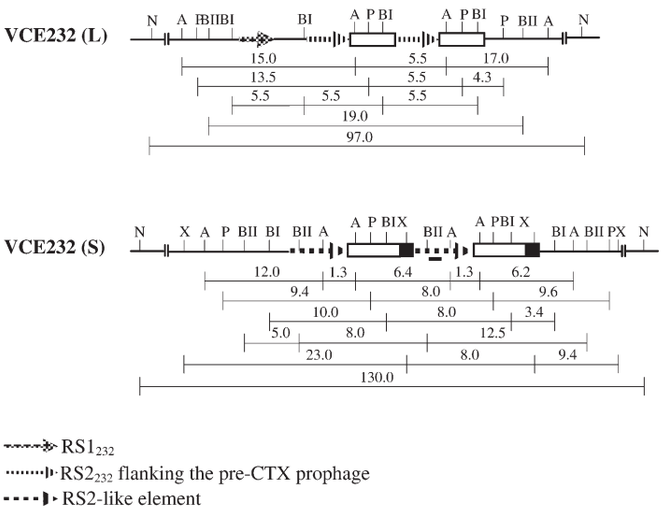


Fig. 6. Schematic representation of the genetic organization of pre-CTX and CTX prophages in the large (L) and small (S) chromosomes of the strain VCE232, respectively. Various restriction fragment sizes (in kb) obtained by hybridization experiments are indicated below each of the genetic organization of prophage. Rectangular box represents truncated core devoid of ctxAB genes. Filled box indicates *ctxAB* genes. Diverse RS elements present in the strain VCE232 are indicated at the bottom. AvaI, A; BglI, BI; BglII, BII; NotI, N; PstI, P; XbaI, X.

Studies on iciA and dnaA genes of V. cholerae related to chromosomal replication

In our previous work we characterized the large chromosomal ori region of *V. cholerae* (oriCI$_{VC}$) and determine the minimal oriCI$_{VC}$. In *E. coli* a dimeric protein with subunits of 33-kDa called IciA [product of the gene *iciA* (inhibitor for *chromosomal* initiation)] binds specifically to the AT-rich 13-mer repeats of the *oriC* region. It shares amino acid homology with the LysR family of prokaryotic transcription regulators. Apart from IciA, DnaA protein (product of the gene *dnaA*) also binds in this region. Under in vitro conditions, binding of the IciA proteins inhibits replication provided it is added before addition of DnaA proteins. This effect is due to a block of the unwinding of the 13-mer region. However, once this region is opened by DnaA protein, the IciA protein is unable to bind over there and as a result there will be no inhibition of replication initiation. It is to be noted that *E. coli* cells with an insertion mutation in the iciA gene or over expression of iciA does not show a striking phenotype, except that cells with excess IciA protein show a longer lag period when diluted into fresh medium. From the sequence analysis of the oriCI$_{VC}$ regions it was found that the AT-rich 13-mer repeats in *V. cholerae* are not well conserved compared to *E. coli*. Therefore, it was of interest to explore some of the functions of *V. cholerae iciA* and *dnaA* genes. At present both the genes were cloned and the effect of overexpression of these genes in heterogonous (*E. coli*) and homologous (*V. cholerae*) genetic backgrounds will be examined. Initial data on overexpression of iciA indicates its negative effect on growth of *E. coli* and *V. cholerae*.

Molecular basis of survival of V. cholerae under nutritional stress

Earlier we have cloned and mutated the crucial stringent response genes *relA* and *spoT* of *V. cholerae*. Our mutational analysis suggested that the *spoT* gene is essential in *V. cholerae* under *relA*$^+$ genetic background. We also generated several *V. cholerae* △*relA* △*spoT* double mutant strains. Interestingly, unlike *E. coli* △*relA* △*spoT* double mutant, the *V. cholerae* △*relA* △*spoT* strain still accumulated (p)ppGpp molecules under glucose or fatty acid starved condition, which raises the probability that there could be an alternative source of (p)ppGpp production in *V. cholerae* besides RelA and SpoT. Recently, another regulatory factor, called DksA (product of the gene *dksA*), has been identified, which acts as a coreulator in stringent response in bacteria like *E. coli*. DksA is required for control of rRNA transcription by ppGpp in vivo and greatly amplifies inhibition of rRNA promoters by ppGpp in vitro. We have cloned the *dksA* gene and *dksA* single mutant, *relA dksA* double mutant and *relA spoT dksA* triple mutant of *V. cholerae* strains were constructed to understand the roles of these genes in amino acid or glucose or fatty acid starved condition. Role of stringent response genes *relA*, *spoT* and *dksA* will be further explored for their involvement, if any, in quorum sensing, biofilm formation, long-term starvation survival and relation with stationary phase sigma factor gene *(rpoS)* expression. We are also working on the essential GTP binding protein *cgtA* and we have provided evidences by genetic methods that like spoT the *cgtA* gene is also essential in *V. cholerae*. Overexpression of *cgtA* under an inducible promoter showed elongation of *V. cholerae* cells, which was most probably due to defect in chromosome segregation. CgtA depleted strains showed sensitivity towards the replication inhibitor hydroxyurea. The *cgtA* gene is essential in *V. cholerae* even in *relA* negative genetic background. Apart from these studies we are also trying to understand the role(s) of nutritional/metabolic differences between biotypes, classical and El Tor, in the evolution of epidemic clones of *V. cholerae*.

Cold shock response and major cold shock proteins of V. cholerae

There are four csp-like genes coding for the Csp proteins in *V. cholerae*. Among these Csps two major Csps, whose molecular masses were 7.7 kDa (CspA$_{VC}$) and 7.5 kDa (CspV), were identified previously by both one- and two-dimensional gel electrophoresis. We cloned, sequenced, and analyzed the *cspV* gene encoding the major cold-shock protein CspV of *V. cholerae*. Recent studies indicated that the *cspV* gene is substantially induced during infection stage. Cloning of the other csp genes are in progress. Mutational studies on the *cspV* gene of both O1 and non-O1, non-O139 strains are currently being investigated.

Comparative analysis of the genomes of Shigella dysenteriae type 2 and type7 strains

The intron-encoded enzyme *I-CeuI* provides a useful tool for determining the copy number of *rrn* operons, which digests the specific 23S-rDNA sequences present in bacterial rrn operons. The *NotI, XbaI* and *I-CeuI* restriction digestion profiles of PFGE separated genomic DNA of two *Shigella dysenteriae* strains belonging to serotypes 2 and 7 were analyzed and the *I-CeuI* linkage maps of the two strains were constructed to investigate their relatedness with the two whole genome sequenced strains *S. dysenteriae* type 1 and *S. flexneri* type 2a. Although the non-type 1 strains are having seven numbers of *rrn* operons in their genomes but they showed distinct restriction fragment polymorphism between themselves as well as with the whole genome sequenced strains. Further analysis revealed that both the genome size and the *I-CeuI* linkage map of the type 7 strain were very close to that of the type 1 strain, while the genome of type 2 strain was very similar to that of *S. flexneri* type 2a strain in these respects. The present study indicates that the *S. dysenteriae* type 7 strain was probably originated from same precursor strain from which the type 1 had evolved, but the type 2 strain had probably generated from same lineage from which *S. flexneri* type 2a has evolved.

Dr. Tripti De

Protective efficacy of galactose terminal glycoconjugates of Leishmania donovani promastigotes

Surface antigens on *Leishmania* promastigotes and infected macrophages are obvious targets in immunoprophylaxis for leishmanial infection. The galactose terminal glycophosphosphingolipid (GSPL) antigen isolated from *Leishmania donovani* surface membrane was recognized by sera from patients with visceral leishmaniasis. GSPL was also expressed on the membrane of parasite infected macrophages (Fig. 7). The effect of GSPL on the production of reactive oxygen species (ROS) and reactive nitrogen intermediates (RNI) was studied using PBMCs isolated from healthy individuals. In addition, induction of IFNγ, IL4, IL10, IL12 secretion in presence of GSPL was investigated. ROS and RNI in addition to IFNγ and IL12 were induced by GSPL. Though there was a moderate induction of IL10, there was very little induction of the Th2 cytokine IL4. The data suggests that this functionally important antigen of *L. donovani* may be used as a candidate vaccine.

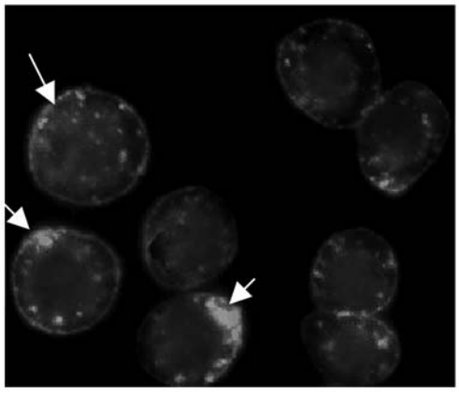


Fig. 7. Fluorescence micrographs of infected macrophages treated with anti-GSPL antibody followed by incubation with FITC conjugated secondary antibody. Arrow indicates the presence of GSPL on macrophage surface.

Developmentaly regulated galactosyltransferase, galactose terminal glycoconjugates and attenuation of Leishmania donovani promastigotes

Modifications of surface glycoconjugates with the expression of terminal galactose residues and evolution of an enzyme, galactosyltransferase (GalT), is probably associated with *Leishmania donovani* attenuation. RT-

PCR using β1-4 galactosyltransferase specific primers revealed a single 360 bp mRNA only in the avirulent clone. Expression of β1-4 GalT in the attenuated atypical *Leishmania* parasite UR6 indicated that the association of the enzyme with virulence attenuation is probably a general phenomenon. The 360 bp product showed 77% sequence identity with *L. major* Friedlin strain, chromosome 13. This product also showed high degree of sequence identity with other known β1-4 GalTs. The predicted translated protein was homologous to other known β1-4 GalTs and a hypothetical protein present in chromosome 13 of *Leishmania major.* The galactosyltransferase gene of the attenuated parasite was sequenced.

Dr. Uday Bandopadhyay

Molecular characterization and functional validation of putative proteins from Plasmodium falciparum proteome: Over expression, purification and localization of putative apoptosis related protein (PfARP) from Plasmodium falciparum

A growing body of evidence has ascertained that apoptosis is not only restricted to metazoans but also exists in unicellular parasites. In *P. falciparum*, the presence of a putative gene having sequence homology with apoptosis related protein (PfARP) (Gene ID PFI0450c) has raised enormous interest to unravel the function of this unique protein in cell death of malaria parasite. PfARP is located in chromosome 9, which contains seven exons together harboring an open reading frame of 495 bp encoding for 164 amino acid protein. To characterize this protein, the PfARP gene has been amplified from the *P. falciparum* transcriptome by RT-PCR and the amplified gene has been successfully cloned, over-expressed and purified to homogeneity. The purified PfARP exhibits minimum subunit MW of ~24 kDa as evident from SDS-PAGE. CD analysis reveals that the β and α content of the recombinant PfARP are 61% and 15%, respectively. Semiquantitative RT-PCR analysis indicates the expression of PfARP at both metabolically less active ring and highly active trophozoite stages of malaria parasite. Immunofluorescence microscopy further supports that PfARP expresses stage specifically with the highest expression at trophozite stage and very little in the schizont stage. PfARP is a cytosolic protein as evident from immunofluorescence microscopy [Protein Expr. Purif. 52: 363-372, 2007]. The role of this protein in *P. falciparum* cell death and stage progression is not yet known. The identification, purification and characterization would certainly be a step to initiate work on this protein to evaluate its role in *P. falciparum* growth, multiplication and stage progression.

Hexadecyltrimethylammonium bromide (HDTAB) offers antimalarial activity through the inhibition of Plasmodium falciparum choline kinase (PfCK)

Generation of phosphocholine by choline kinase is important for phosphatidylcholine (PC) biosynthesis via Kennedy pathway and PC biosynthesis is essential for intraerythrocytic growth of malaria parasite. In addition, choline kinase also plays a pivotal role in trapping essential polar head group choline inside the malaria parasite. Therefore, PC biosynthesis has been suggested as a realistic target for development of new pharmacophores even against pharmacoresistant strain. Choline kinase (CK) catalyzes the initial step in the CDP-choline pathway and can be regulatory for PC biosynthesis in various biological systems. But so far the regulatory role of CK has not been reported in malaria parasites, although a positive correlation between intracellular phosphocholine pool and PC content had been found under certain quaternary ammonium compound treatment, indicating CK may have the potential to regulate PC biosynthesis in malaria parasite also. A putative gene (Gene ID PF14_0020) in chromosome 14, having highest sequence homology with choline kinase has been identified by BLAST searches from *P. falciparum* genome sequence database. Recently, we have cloned, over-expressed and purified *Plasmodium falciparum* choline kinase (PfCK) [Biochem. Biophys. Acta. 1760: 1027-1038, 2006]. But the function of this enzyme in parasite growth and survival has not been evaluated owing to lack of suitable inhibitor. Moreover, this well characterized PfCK may be exploited in the screening of new choline kinase inhibitors to evaluate their antimalarial activity.

Purified recombinant PfCK enabled us to identify an inhibitor of PfCK, hexadecyltrimethylammonium bromide (HDTAB), which has very close structural resemblance to hexadecylphosphocholine (miltefosin), the well-known anti-proliferative and anti-leishmanial drug. HDTAB dose dependently inhibited PfCK and offered very potent antimalarial activity in vitro against *Plasmodium falciparum*. Moreover, HDTAB exhibited profound antimalarial activity in vivo against rodent malaria parasite *Plasmodium yoelii* (N-67 strain). Interestingly, parasites at trophozoite and schizont stages were found particularly sensitive to HDTAB. The stage specific antimalarial effect of HDTAB correlated well with the expression pattern of PfCK in *P. falciparum*, which was observed by RT-PCR and immunofluorescence microscopy. Furthermore, antimalarial activity of HDTAB paralleled with the decrease in phosphatidylcholine content, which was found, correlated with the decreased phosphocholine generation. These results suggest that inhibition of choline kinase by HDTAB leads to decreased phosphocholine, which in turn causes decrease in phosphatidylcholine biosynthesis resulting in death of the parasite [Antimicrob Agents Chemother. 51:696-706, 2007].

Dr. Mridula Misra

Development of new radiopharmaceuticals for nuclear brain imaging: Pharmacokinetics and mechanism of action

a) Entrapment of 99mTc chelate complexes into liposome and their biodistribution studies in Sprauge-Dawley rat.

The 99mTc chelate complexes of cysteine methyl ester, cysteine ethyl ester, cystine dimethyl ester, and cystine diethyl ester prepared by $SnCl_2$ method, are entrapped in liposome. The liposome is prepared by Phospatidyl Cloline and cholesterol. Entrapment efficiency was measured by sucrose gradient method.

In-vivo distribution study of the liposome entrapped 99mTc chelate complexes were performed in Sprauge Dawley rat. A significantly increased brain uptake was observed with the liposome entrapped 99mTc chelate complexes as compared with the unentrapped complexes. The normal biodistribution showed an enhanced uptake of liposome entrapped 99mTc chelate complexes in rat brain but shows comparatively less uptake in the ischemic rat brain. Imaging studies have been started with the above mentioned complexes under the gamma camera at Thakurpukur Cancer Research Centre, Kolkata.

b) Effect of plant extract on the biodistribution of radiopharmaceuticals. The effect of *baccopa monniera* (BM) extract on the Biodistribuion studies of 99mTc chelate complexes of cystine dimethyl ester and ECD (ethyl cysteinate dimer) in normal and ischemic (by common carotid artery occlusion (CCAo)) rat was studied. In this study it was found that BM plant extract treated group of animals significantly increase the uptake of 99mTc-ECD and 99mTc-cystine dimethyl ester in brain, liver, kidney and lungs with respect to control (untreated) group of rats. The effect of BM extract on the labelling of blood elements was also studied. Further research work of drug (synthetic/natural) effect on different organ uptake of radiopharmaceuticals are in progress.

As a Radiation Safety Officer implemented the Radiation Safety aspects in Research application of Ionizing Radiation; booklets "Radiation Safety Guideline" and "Guidelines for Chemical Safety" have been prepared for the safe use of radioisotopes in IICB. Procured & distributed radioactive materials for research from BARC, Mumbai & abroad like Amersham, NEN etc. Provided maintenance of the Central Radioactivity Facility of IICB, TLD badge service and radioactive waste disposal facility for the radioisotope users in IICB.

Dr. Mita Chatterjee Debnath

Rapid diagnosis of myocardial cell damage with 99mTc- S-thiomethyl cysteine

S-thiomethyl a novel protecting group developed from this laboratory, for masking the high reactivity of thiolate function attached to different 99mTc- binding ligands and can be removed instantaneously and quantitatively during chelation. These findings led to the development of 99mTc S-thiomethyl cysteine chelate. After thorough physico-chemical characterization (TLC, HPLC etc.) the chelate has been studied in acutely damaged rat heart model. The damage has been initiated by ligating the left anterior descending coronary artery of the animal as detected by ECG changes. (Fig. 8).The chelate exhibited definite uptake in damaged rat myocardial model. The damage has been identified by scintigraphic & autoradiographic detection and histologic changes (Fig. 9)

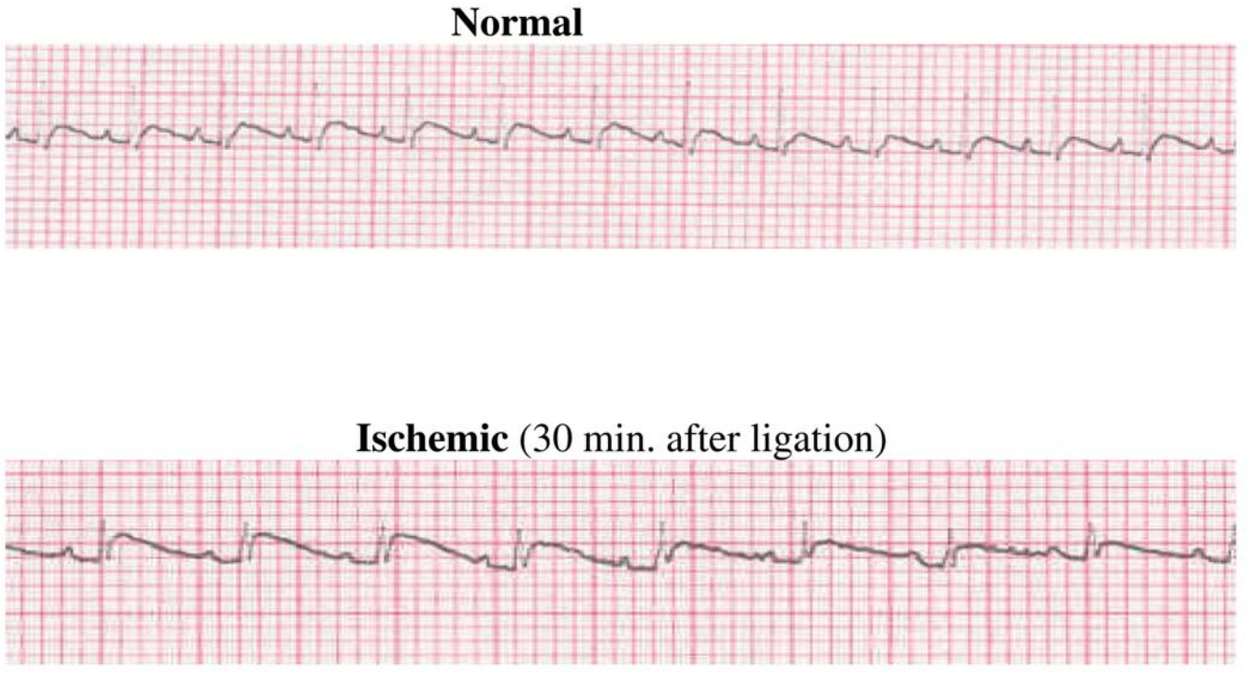


Fig. 8. Electrocardiograms.

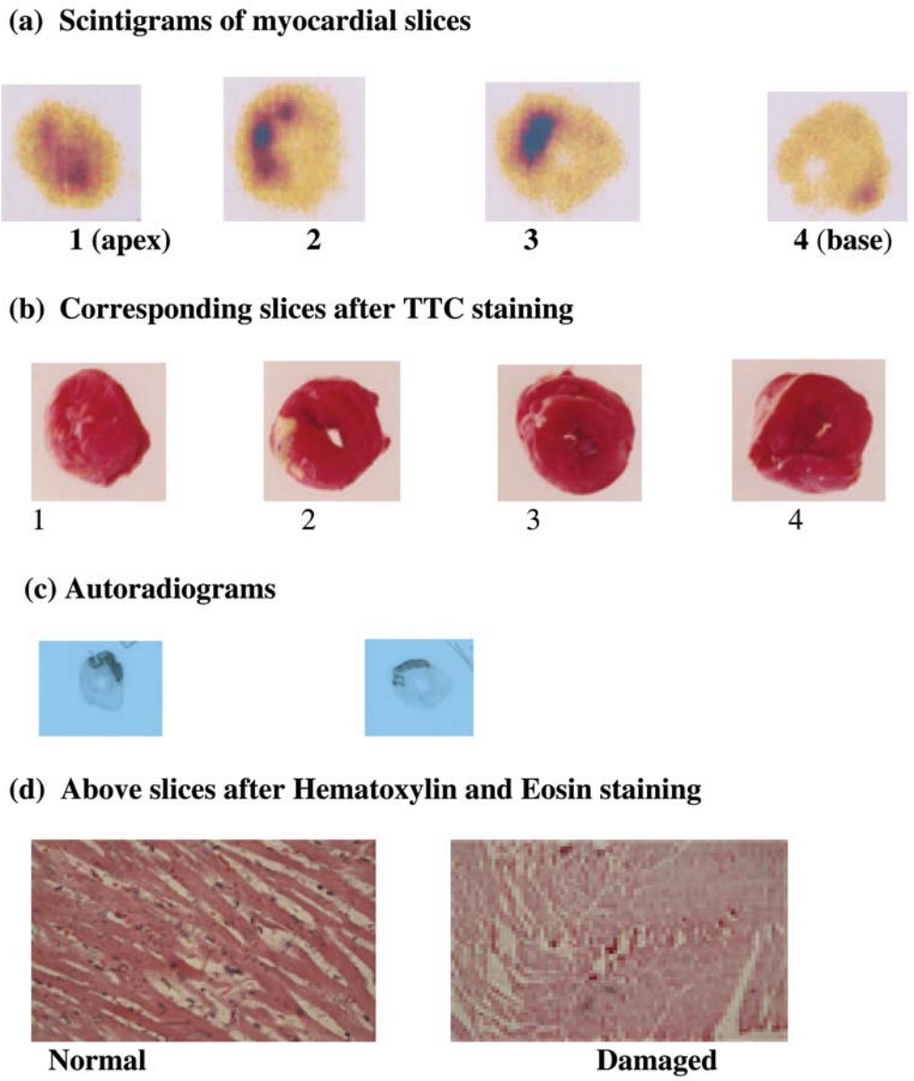


Fig. 9. (a) Scintigrams and (c)autoradiograms obtained after 99mTc-S-thiomethyl cysteine injection in rat model subjected to 1hr corhonary ligation. The damage has been corroborated by (b) TTC staining and (d) light microscopic examination after hematoxylin and eosin staining of myocardial specimen.

Upgradation of major infrastructural facilities

Dr. Rupak K. Bhadra

Establishment of Scanning Electron Microscope (Tescan, Model VEGA II LSU) Facility with EDS system.

Technical Officers

Dr. Kalidas Paul, Mr. Rabindra Nath Mandi, Mrs. Arti Khetrapal, Mr. Asish Mallick, Mr Kshudiram Naskar, Mr. Pratap C. Koyal.

Technical Staff

Mrs. Rita Maity, Mr. Anirban Manna, Mr. Avishek Mukherjee

Pool Officers, RAs, Research Fellows etc.

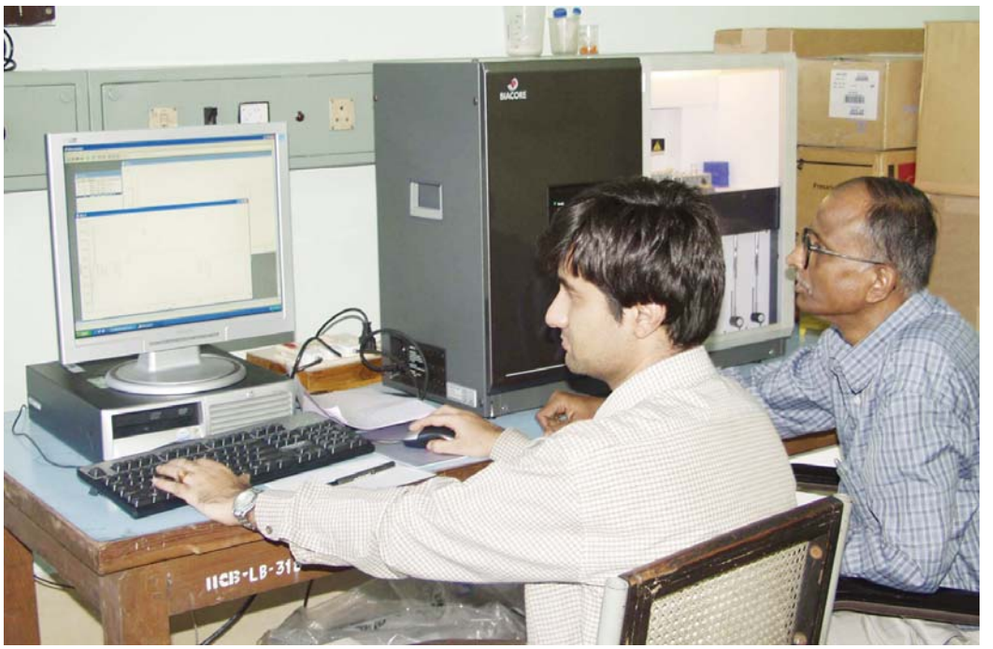
Dr. (Mrs.) Neeta Dutta, Dr. (Ms.) Saswati Laha, Dr. Tapasi Das, Dr. Anindita Bhattacharya, Dr. Rajatava Basu, Dr. (Mrs.) Monidipa Ghosh Ray, Dr. Tanusree Das, RA, Dr. (Mrs.) Kakai De, Mr. Agneyo Ganguly, Mr. Somdeb Bose Dasgupta, Mrs. Rakhee Das, Mrs. Bijoylaxmi Banerjee, Mr. Souvik Sengupta, Mr. Amit Roy, Aruna Biswas, Snigdha Mukherjee, Arijit Bhattacharya, Sudipta Pal, Susanta Kar, Arunima Biswas, Waliza Ansar, Suchandra Chowdhury, Chandan Mandal, Angana Ghoshal, Susmita Mandal, Sajal Samanta, Mr. Rajan Guha, Mr Ranjan Dhar, Ms June Ghosh, Ms. Moumita Ghosh, Ms. Shubha Sen, Dr Suniti Bhawmick, Mrs. Jayashree Bagchi Chakrabarty, Dr. Labanya Mandal, Mr. Kausik Paul, Mr. Nabendu Biswas, Mr. Surjendu Bikash Debnath, Ms. Arpita Chatterjee, Ms. Sohini Chaudhuri, Mr. Amalendu Ghosh, Ms. Abha Bhagat, Mr. Amit De, Ms. Epshita Chatterjee, Mr. Amit K. Baidya, Mr. Bhabotosh Das, Ms. Sangita Shah, Mr. Ritesh Ranjan Pal, Mr. Kalpataru Halder, Mr. Siddhartha Kumar Bhaumik, Mr. Manoj Kumar Singh, Mr. Subir Karmakar, Mr. Kamal Krishna Halder, Sumita Pal, Sarmistha Majumder, Archana Patra, Jayeeta Roychoudhury, Antara Banerjee, Sudipta Bhowmick, Partha Palit, Smriti Mondal, Saumyabrata Mazumdar, Manjarika De, Mithu Guha, Pallab Maity, Susmita Chandra

Administrative Staff

Mr. Dipak Guin, Mrs. Moumita Majumdar

Lab Attendant

Mr. Narendra Pradhan, Mr. Biswajit Mandal




APOPTOSIS:
MECHANISM of
CELL DEATH

Cell Biology & Physiology

Drs. K. P. Mohanakumar, Sumantra Das, S. N. Kabir, Smritinath Chakraborty, Tuli Biswas, Chhanda Mitra, Arun Bandyopadhyay, Tushar Chakraborty, Sandhaya R. Dungdung, Sib Sankar Roy, Padma Das, Mrinal Kanti Ghosh

CELL BIOLOGY

Dr. Tuli Biswas and group

Structural and functional changes in erythrocytes during anemia in visceral leishmaniasis

Visceral leishmaniasis (VL) is associated with reduced survival of erythrocytes. The mechanism underlying the shortened lifespan of red blood cells (RBC) has been studied and a combination therapy with quercetin (Qr) and serum albumin (SAlb) has been proposed towards its rectification in this disease.

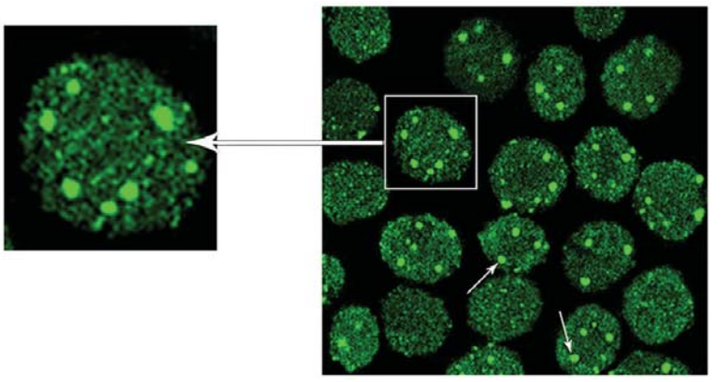


Fig. 1. Band 3 colocalization on erythrocytes from infected hamsters. Bright spots represent dense clusters of band 3 on red cell membrane, view as under confocal microscope. Magnification: 1000 X; inset enlargement: 2300 X.

Decreased redox potential in RBC followed by oxidative denaturation of hemoglobin (Hb) and pathologic association of iron with cell membrane facilitate premature hemolysis in VL. Oxidative denaturation leads to the release of heme moiety from globin. Increase in the fluorescence intensity of Hb tryptophan during infection from the control level reflects a decrease in fluorescence quenching effect of heme on globin and is due to the departure of heme from globin. The cytosolic face of RBC membrane has been found to carry abnormal iron compartments in the form of heme and nonheme iron. Attempt to determine the location of heme iron evince its firm alliance with the membrane lipid core. Our results further show the association of chelatable nonheme iron with the polar head group of aminophospholipids. This cellular iron decompartmentalization is responsible for the iron mediated targeting of oxdidative damage to the membrane structures. Enhanced interaction between denatured globin and cytoplasmic domain of band 3 induces colocalization of band 3 (Fig. 1) leading to autologous IgG binding and consequent erythrophagocytosis in VL.

Qr, a bioflavonoid is widely distributed throughout the plant kingdom and possesses a variety of pharmacological activities. We have previously reported the therapeutic efficacy of Qr in premature hemolysis in VL. Since SAlb functions as the principal carrier protein for Qr, development of hypoalbuminia in VL reduces the potency of Qr against this disease. Simultaneous treatment with Qr and SAlb favor the interaction between the two under in vivo condition (Fig. 2). This increases the bioavailability of the flavonoid, leading to its greater delivery to the target sites and equips the combination to have an advantage over Qr alone, in increasing red cell survival in VL.

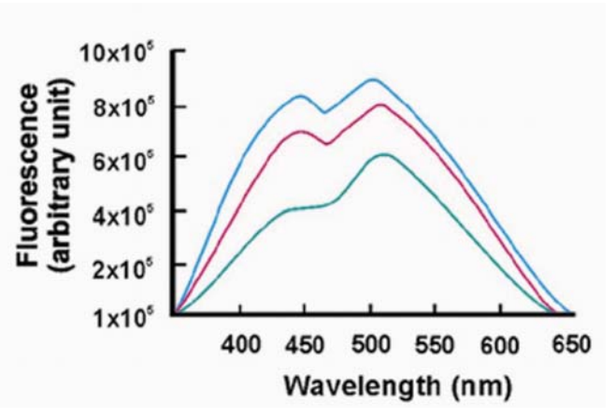


Fig. 2. Interaction between Qr and SAlb on the fluorescence emission spectra of Qr. SAlb modulated emission intensity of Qr in infected animals. Control (blue), infected (green) and Qr + SAlb treated infected (red).

Studies on the mechanism of hemolysis in chronic arsenic toxicity

Arsenic contamination of drinking water is one of the biggest natural calamity affecting India and Bangladesh. Abbreviation of erythrocyte life span and the development of anemia is a common sequel in chronic exposure to arsenic. Normal structural matrix permits RBC to undergo a reversible deformation as a viscoelastic material and perturbations in membrane components can lead to the development of hemolytic disorders. A collaborative study with Dr. A.K. Giri of Human Genetics and Genomic group has been undertaken with an objective to assess the influence of conformational changes in erythrocytes on the development of anemia in chronic arsenic exposure.

Arsenic disturbs the membrane curvature of smooth discoid human RBC and transforms them into evaginated echinocytic form. Further distortion converts reversible echinocytes to irreversible spheroechinocytes (Fig. 3), ultimately making the cells susceptible to hypotonic lysis. Arsenic toxicity hampers the flexibility of normal cell membrane by changing the spatial arrangement of membrane proteins and disrupts spectrin-actin-band 4.1 lattice of the cytoskeleton. Loss of phospholipid asymmetry along with the increase of cholesterol / phospholipid ratio indicates decreased RBC deformability which is further confirmed from the decreased fluidity of RBC membrane in the exposed population. This study shows the involvement of distorted cytoskeletal protein framework and altered membrane lipid dynamics in the destruction of erythrocytes during chronic arsenic exposure.

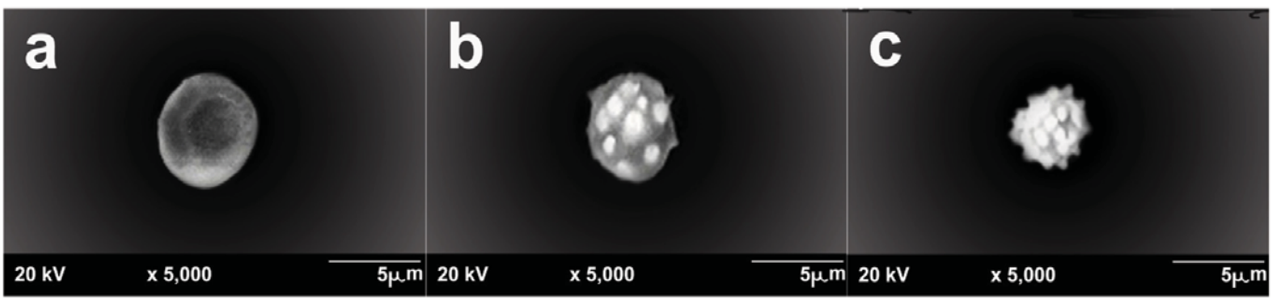


Fig. 3. Arsenic induced conformational changes in erythrocytes. Scanning electron micrographs showing the transformation of normal discocyte to spheroechinocyte during arsenic exposure. (a) Discocyte, (b) Echinocyte and (c) Spheroechinocyte. Magnification: 5000 X.

MOLECULAR ENDOCRINOLOGY

Dr. Arun Bandyopadhyay and group

Dexamethasone alters expression of the genes for Ca^{2+} release channels leading to the cardiac dysfunction in rat

Although glucocorticoid is well known antiinflammatory drug, its use is often limited due to various side effects including cardiovascular complications. The present study was undertaken to understand the mechanism of contractile abnormality by excess of glucocorticoid. Treatment of rat with synthetic glucocorticoid, dexamethasone (35 µg/100 g BW) resulted in increase in heart weight to body weight ratio (HW/BW), expression of atrial natriuretic peptides mRNAs with the duration of treatment up to 15 days. The end systolic and end diastolic pressure were significantly increased and cardiac contractility was significantly decreased after 15 days of dexamethasone treatment compared to those of control rats. The level of AT1 receptor in left ventricular tissue was increased compared to control and mifepristone inhibited such alteration. Dexamethasone dramatically increased the expression of the subunits of the L type Ca^{2+} channels and calsequestrin in LV tissues compared to control. Co-treatment of mifepristone with dexamethasone significantly prevented alteration of both L Type Ca^{2+} channels and calsequestrin compared to control. The expression of SERCA was significantly reduced in dexamethasone treated samples. The level of junctin mRNA was significantly reduced by dexamethasone and co-treatment with mifepristone did not restore it to the level of control tissue. Dexamethasone also increases the cell size of the neonatal rat ventricular cardiomyocytes (NRVM) and expression of ANP, BNP, subunits of the L type Ca^{2+} channels and calsequestrin -mRNAs after 24 h of treatment which was mostly blocked by mifepristone. The spontaneous Ca^{2+} oscillations in NRVM was reduced by DEX compared to control cells. Stimulation of cardiac myocytes with caffeine induces sharp and transient Ca^{2+} release which was altered and prolonged in the dexamethasone treated cells. These effects are partially restored by mifepristone when co treated with dexamethasone. Taken together, these data show that abnormal handling of intracellular Ca^{2+} may be responsible for decreased contractility of heart in dexamethasone treated animal. The results are important to understand the pathophysiology of heart in the patients treated with excess of glucocorticoid.

Regulation of extracellular matrix in hypertrophied myocardium due to excess of glucocorticoid

To understand the mechanism of cardiac malfunction due to excess of glucocorticoid, regulation of myocardial extracellular matrix and collagen deposition were examined in rat treated with synthetic glucocorticoid, dexamethasone (DEX). Heart weight/body weight ratio was significantly increased with the duration of DEX (35 g/100 g BW) treatment up to 15 days compared to vehicle treated control which was unchanged when animals were co-administered with mifepristone (MIF), a glucocorticoid receptor antagonist. The expression of atrial natriuretic peptide in ventricular tissues was also increased by DEX which was reduced by MIF. Collagens deposition in the ventricular tissues was increased in rats treated with DEX compared to control. While expressions of procollagens I and III were reduced, the level of mature collagens I and III was significantly increased in the ventricular tissues of rats treated with DEX as compared to the control. The expression of matrix metalloproteinases I and 13 was decreased in ventricular tissues by DEX compared to the control. The activity of both matrix metalloproteinases I and 13 was significantly ($P<0.01$) reduced and that of MMP2 was significantly increased in the serum of DEX treated rats compared to control. The levels of tissue inhibitor of metalloproteinases type 3 and 4 remained relatively unchanged in the DEX treated rat left ventricle. These data show that glucocorticoid induces collagen deposition and fibrosis in heart which is differentially regulated by matrix metalloproteinases. These results are important to understand the pathophysiological significance of excess of glucocorticoid cardiovascular system.

Predictive medicine using repeat and single nucleotide polymorphisms

The genes under study, in this mission mode project, are Calsequestrin 2 (cardiac type) [CASQ2], Troponin I [TNNI3], Troponin T [TNNT2], Potassium channel [KCNH2], Troponin C [TNNC], Actinin [ACTN1]. Of these, details of genes submitted for sequencing are [CASQ2], [TNNI3], [TNNT2] and [KCNH2]. SNPs found in these genes are as follows:

DSNP No	#SNP rs#	chr no.	Gene(s)	Position on Chromosome (bp)	Role	Alleles	Amino acid change
CASQ2 (total-6SNPs)							
NA	rs4074536	1	CASQ2	1.16E+08	1_EXON	C/T	T/A
NA	rs10754351	1	CASQ2	1.16E+08	1_INTRON	A/G	-
NA	rs10754355	1	CASQ2	1.16E+08	1_INTRON	A/G	-
NA	rs4240550	1	CASQ2	1.16E+08	1_INTRON	G/T	-
NA	rs4564143	1	CASQ2	1.16E+08	1_INTRON	C/T	-
NA	rs9428087	1	CASQ2	1.16E+08	1_INTRON	A/G	-
TNNI3 (total-4SNPs)							
NA	rs2278281	19	TNNI3	60360009	2_INTRON	A/C	-
NA	rs3729838	19	TNNI3	60360122	2_INTRON	C/G	-
NA	rs2288528	19	TNNI3	60359312	4_INTRON	A/T	-
NA	rs3729841	19	TNNI3	60357222	6_EXON	A/G	E/E
TNNT2 (total-4SNPs)							
NA	rs11806184	1	TNNT2	2E+08	11_INTRON	C/T	-
NA	rs868407	1	TNNT2	2E+08	2_INTRON	C/T	-
NA	rs10920183	1	TNNT2	2E+08	4_INTRON	A/G	-
NA	rs3729547	1	TNNT2	2E+08	9_EXON	C/T	I/I

Asthmatic and allergic disorders mitigation mission

Phosphodiesterase 4 (PDE 4) is one of the key enzymes involved with the pathophysiology of asthma. Therefore efforts are going to identify lead molecule both from herbal as well as synthetic sources which would selectively inhibit PDE 4B. Ten molecules two natural and eight synthetic' (ICB11-D6,ICB11-D8, ICT52, ICT55, ICT57, ICT67, ICT83, ICT97, ICT100, ICT102) inhibited PDE 4 activity. These molecules will be tested for the in vivo efficacy for managing asthma in rodent model during 11th FYP.

Dr. Sib Sankar Roy and group

The role of Pitx2 homeodomain transcription factor in ovarian development and its function

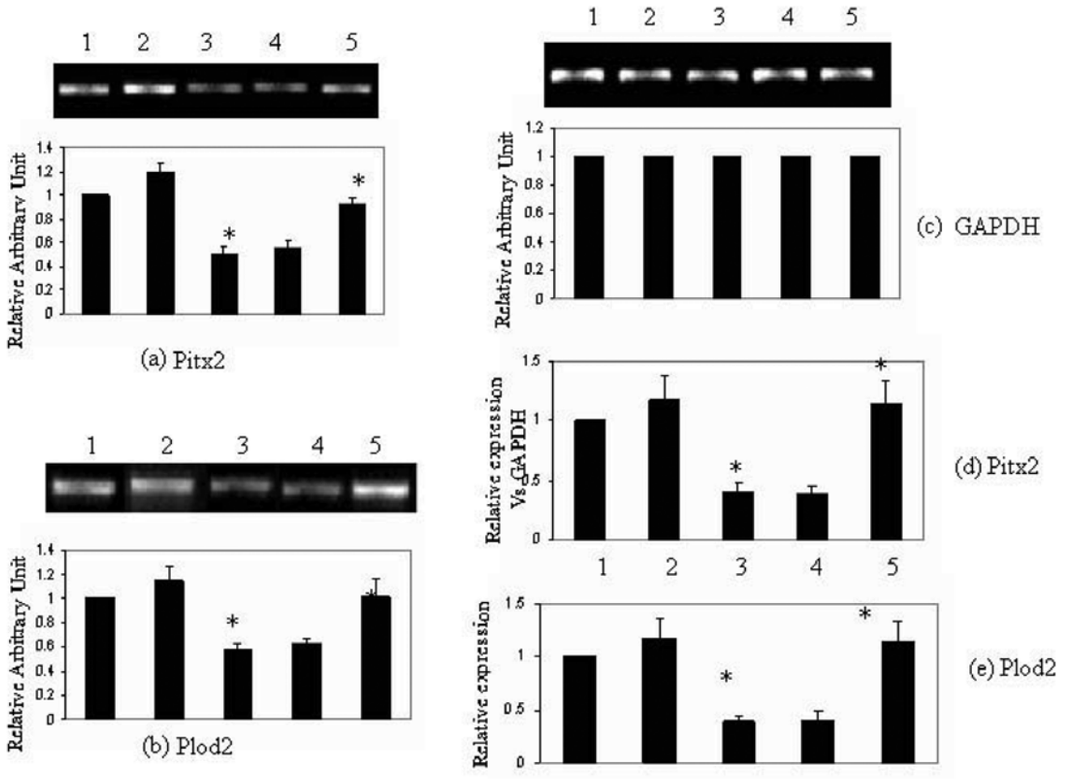


Fig. 4. RT-PCR (Fig a, b, c) and QPCR data (Fig d, e) show the efficiency of Pitx2 siRNA in knocking down the expression level of Pitx2 itself and also in turn of Plod2 gene. In Fig a, Pitx2 expression level has been shown in mock transfected SK-OV3 cells (lane1), negative siRNA transfected cells (lane 2), Pitx2 specific siRNA transfected cells after 48 hrs (lane 3). Lane 5 shows Pitx2 expression level when T3 was added to the medium for 3 hrs after 45 hrs of Pitx2 siRNA transcription respectively, whereas no T3 was added in the 45 hrs transfected cell culture medium (lane 4). In Fig. b and c, RT-PCR data shows the expression level of Plod2 and GAPDH gene under the above-mentioned condition. In Fig. d and e, Q-PCR data show that the expression level of Pitx2 gene is in the same order of transfected cells as mentioned in Fig. a (lanes 1-5).

Our group has shown the expression of Pitx2 gene, a bicoid related homeodomain transcription factor in ovarian tissue of rat and human and its function in this tissue has been partially identified. Pitx2 plays an obligatory role to transcriptionally regulate the hormone genes, like LHβ, FSHβ, PRL in pituitary and Plod2 in mice brain. In our previous report we showed that Plod2 was down regulated in hypothyroid rat ovary resulting in loss of ovarian structural integrity. In order to study the regulation of Plod2 gene expression in ovary, we looked for the presence of Pitx2 in ovary and showed that it binds to specific bicoid element in Plod2 promoter by EMSA and that it is an upstream activator of Plod2 gene by siRNA mediated gene knock down study (Figs. 4 & 5).

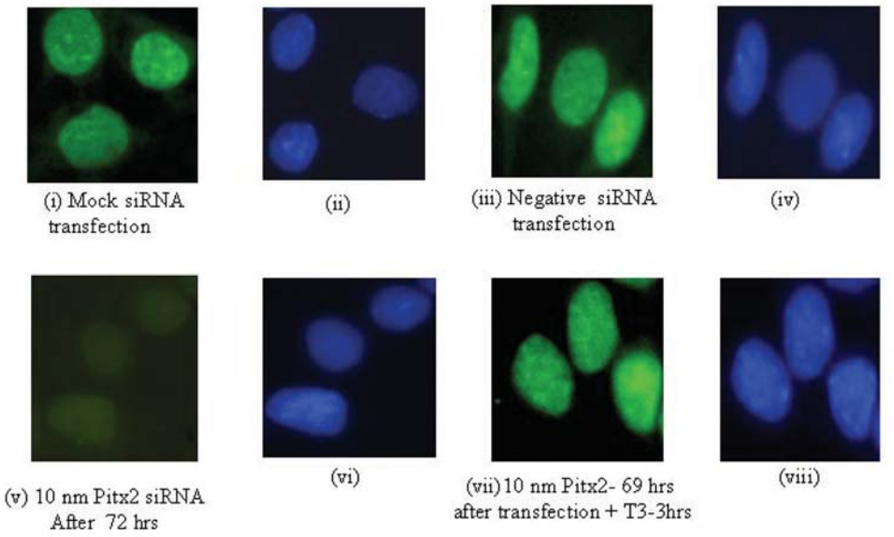


Fig. 5. The immunocytochemistry data. Pitx2-specific fluorescence is shown in the mock transfected cells (i), negative siRNA transfected cells (iii), Pitx2 siRNA-transfected cells (v) and Pitx2 siRNA transfected cells treated with T3 for 3 h after 69 h of transfection (vii). In this Fig., (ii), (iv), (vi) and (viii) represent the corresponding DAPI-stained cells of (i), (iii), (v) and (vii) respectively.

Since Pitx2 is a versatile transcription factor as has been shown earlier, we were interested to know other functions that it plays in ovary by targeting different genes and following pathways that are still unidentified. Besides maintaining ovarian structural integrity, Pitx2 is essential for cellular proliferation and it is a transcriptional regulator of crucial cell cycle regulatory genes, like, cyclin D2 and c-myc in ovary. By chromatin immunoprecipitation followed by micro-array analysis (ChIP-chip) we have identified gene profiles that are probable target of Pitx2. Characterization of these genes is in progress. To execute its diverse transcriptional regulation of different genes, Pitx2 needs different cofactors. By co-immunoprecipitation, we have identified the cofactors that are associated in ovary to regulate different genes (Fig. 6). As in other tissues, Pitx2 could be inevitable for ovarian development, too. At different days of ovarian development the tempoaral and spatial expression profile of Pitx2 and its binding and stage-specific transactivation of different key genes are being investigated. Detail information on transcriptional regulation of different target genes of Pitx2 will be very much useful for understanding the pathophysiology of ovarian tissue and for further therapeutic application.

Hypothyroidism associated ovarian disorders: a molecular and biochemical study

Hypothyroid induced reproductive malfunction in both the sexes is a common phenomenon of global concern. To know the molecular basis of this disorder, we have identified several genes that are responsible for ovarian dysfunction in some way or other. We have shown the role of lysyl hydroxylase and matrix metalloproteases in collagen metabolism in ovarian tissue in normal and hypothyroid condition (Saha et al, Endocrinology, 2005). Apart from their role in ovarian dysfunction, we have investigated the regulation of expression of these genes by thyroid hormone. The results indicate that in hypothyroid condition collagen biosynthesis in ovary seems to be disturbed with concomitant enhancement in collagen degradation resulting in disintegration of overall ovarian structure.

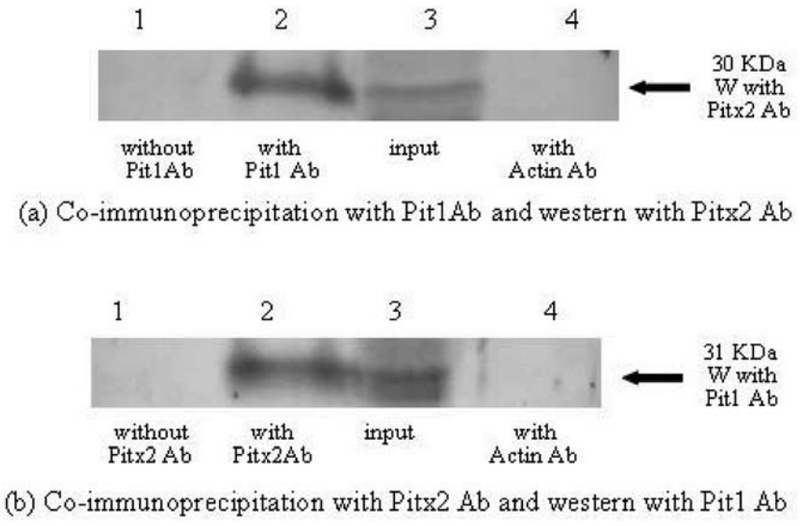


Fig. 6. Association of Pit1with Pitx2 in rat ovary as evident from co-immunoprecipitation. In co-immunoprecipitation reaction (a), ovarian proteins were pulled down in absence of any antibody (lane 1), with Pit1 Ab (lane 2), input control (lane 3) and with actin Ab (lane 4) and then electrophoresed, transferred onto PVDF membrane and then immunodetected with Pitx2 Ab. Similarly, in Fig b, the blot was immunodetected with Pit1 Ab, where ovarian proteins were pulled down in absence of any Ab (lane 1), with Pitx2 Ab (lane 2), input control (lane 3) and with actin Ab (lane 4) followed by electrophoresis, transfer onto PVDF membrane and then immunodetection with Pit1 Ab. The molecular weights of the proteins are denoted with arrow.

We have shown the expression of collagen II (Fig. 7) in ovarian tissue (Saha et al, Cell Physiol Biochem, 2007a) and it is the most affected collagen in hypothyroid condition. In hypothyroidism, collagen II degrading MMPs are up-regulated in ovary. Therefore, the rate of its degradation is much higher in this condition. To further investigate the factors that play important roles in hypothyroid associated ovarian dysfunction, we have shown that HSP-47 (chaperone for collagen in ovary) and Prolyl 4 hydroxylase are up-regulated in hypothyroid ovarian tissue (Saha et al, Cell Physiol Biochem, 2007b). We hypothesize that as Lysyl hydroxylase is down-regulated, P4H and HSP47 are up-regulated to compensate the maturation of procollagens in hypothyroid condition; further investigation is in progress now.

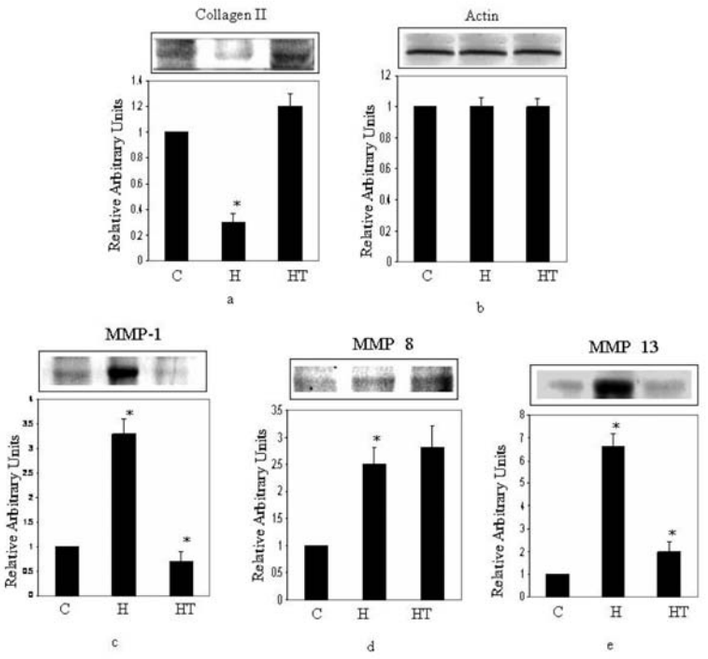


Fig. 7. Status of Col II, MMP-1, MMP-8 and MMP-13 in hypothyroid condition. 30μg of total ovarian proteins from each set were fractionated on 10% SDS-polyacrylamide gel, transferred onto PVDF membrane and subjected to immunodetection with goat anti-collagen II (a), mouse anti-MMP-1 (c), goat anti-MMP-8 (d), goat-anti-MMP-13 (e) antibodies and mouse anti β-actin antibody as an internal control (b). The lanes indicating 'C', 'H', and 'HT' represent the protein loaded were isolated from control, hypothyroid and T3 injected hypothyroid animals respectively. The protein bands were quantified with ImageJ software (NIH, USA) and the lower panels of the respective figures show the pixel densities of the protein bands represented by relative arbitrary unit (RAU). The experiments were performed three times in duplicate and the mean ± SD values have been shown. *, P< 0.05.

Another aspect of our study is the role of neuropeptide-tachykinin in ovarian function. Tachykinin levels in plasma are known to be altered with sexual acyclicity and loss of reproductive function. Our group has observed differential expression of tac2 along with other tk genes and their receptors in rat pituitary and ovary along with human ovary, which suggests that hypothyroidism affects the expression of these genes in these tissues (Ghosh et al, Cell Physiol Biochem, 2007). Significant reduction of tac2 expression in reproductively less active rat ovary suggests the association of tac2 with reproductive senescence. Our results cumulatively suggest that decline in reproductive function in hypothyroidism is associated with altered expression level of tac2 and its receptors. Further investigation in this area could elucidate the possible mechanism of tachykinins' involvement in loss of sexual cyclicity and other reproductive disorders associated with hypothyroidism.

Hence, to understand the genetic, molecular and biochemical basis of hypothyroid induced reproductive disorders, we have identified and characterized several significant genes. We are also trying to find out the role of other related genes in these disorders. Detailed study of which may provide useful information regarding the cause and therapy of these disorders.

Molecular mechanism of insulin resistance and evaluation of anti-diabetic principles

In this project we investigate the molecular mechanism of insulin resistance. Insulin resistance or loss of insulin signal is a complicated process; it involves many genetic and environmental factors. The detailed mechanism of insulin resistance and diabetes type 2 is not known yet. Free fatty acid (FFA) is one of the major factors linked to the development of insulin resistance and type2 diabetes. However, the underlying mechanism in FFA-induced insulin resistance is not known yet.

We have shown that palmitate causes insulin resistance inhibiting phosphorylation of PDK1; insulin receptor (IR) transcription is also reduced by palmitate, following defect in translocation of PKCϵ (Dey et al, Biochem Biophys Res Com, 2007). Phospho-PKCϵ adversely affected HMGA1; as HMGA1 regulates IR promoter activity,

expression of IR gene is impaired. It causes reduction of IR on cell surface resulting less insulin sensitivity. The role of mitochondria and mitochondrial proteins is important in causing diabetes type 2. We have shown the expression profiles of mitochondrial genes that are involved in diabetes type 2. In this regard the role of PGC1α and uncoupling proteins (UCP-2 and -3) is being investigated. Different herbal components are also being screened for their antidiabetic activity by using sensitive biochemical and molecular biological techniques.

NEUROSCIENCE

Dr. K. P. Mohanakumar and group

Neurodegeneration and Neuroprotection

Pathophysiology of neurodegenerative disorders such as Parkinson's disease (PD) and neuroprotective measures are investigated. During the period under report, it has been demonstrated that the dopaminergic neurodegeneration caused by 1-methyl-4-phenylpyridium (MPP^+) in rats, the metabolite of the parkinsonian neurotoxin 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) results from apoptosis.

Apoptotic mode of cell death in MPP^+ model

Nuclear morphology of cells in the substantia nigra pars compacta (SNpc) region of rats has been investigated following unilateral intranigral infusion of the active metabolite, MPP^+. Administration of the neurotoxin resulted in a dose-dependent and prolonged dopamine depletion in the ipsilateral striatum (Fig. 8), and loss of tyrosine hydroxylase immunoreactive neurons in the SNpc (Fig. 9). Specific nuclear staining with Hoechst 33342 or acridine orange revealed bright pyknotic, shrunken, distorted nuclei and condensed chromatin with perinuclear nucleolus respectively following visualization with the former and latter dyes in the ipsilateral SNpc, as compared to the round, intact nuclei and centrally positioned nucleolus in the contralateral side (Figs. 10, 11). Ultrastructural details of the nucleus under transmission electron microscope confirmed distorted nuclear organization with shrunken or condensed nuclei and disrupted nuclear membrane. These features are typical of nucleus undergoing apoptosis, and suggest that MPP^+ causes dopaminergic neuronal death through an apoptotic mode (Fig. 12). Typical laddering pattern of genomic DNA isolated from the ipsilateral SN in agarose gel electrophoresis established apoptosis following intranigral administration of MPP^+ in rats (Fig. 13).

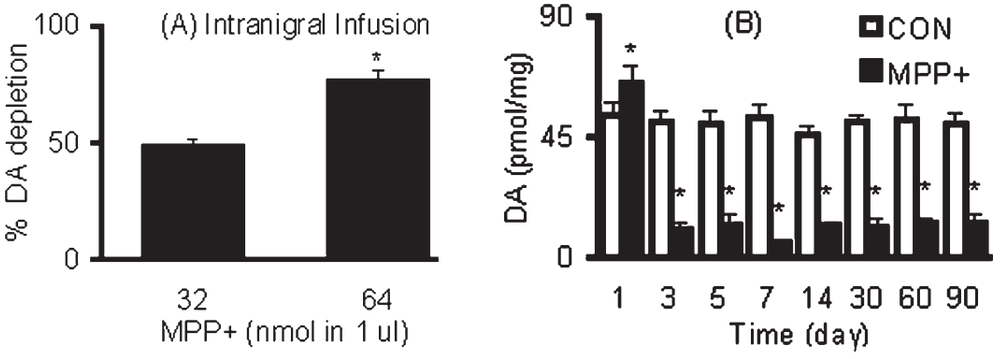


Fig. 8. Effects of intranigral infusion of MPP+ on striatal dopamine (DA) levels. (A) Rats were sacrificed on the 5th day following intranigral infusion of MPP+ (32 and 64 nmol in 1 µl). (B) Animals infused with MPP+ (64 nmol in 1 µl) were sacrificed after 1, 3, 5, 7, 14, 30, 60 and 90 days following the administration of the neurotoxin.

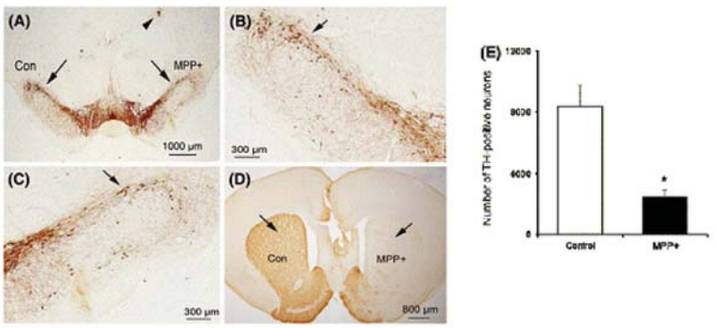


Fig. 9. Loss of TH immunoreactivity in SNpc and NCP as a response to intranigral infusion of MPP$^+$. Representative photomicrographs of coronal sections passing through SN (bilateral layout: A), SN contralateral to the side of infusion (B), SN ipsilateral to the side of MPP$^+$ infusion (C) and NCP (bilateral layout: D). The arrow marks (A-C) indicate the location of SNpc, while the arrowhead (A) shows the needle-track. Arrows in Fig. 9D indicate the contra (left) and ipsilateral (right) NCP. In Fig. 9E are given the numbers of TH positive neurons in the ipsi and contralateral sides of MPP$^+$ infusion.

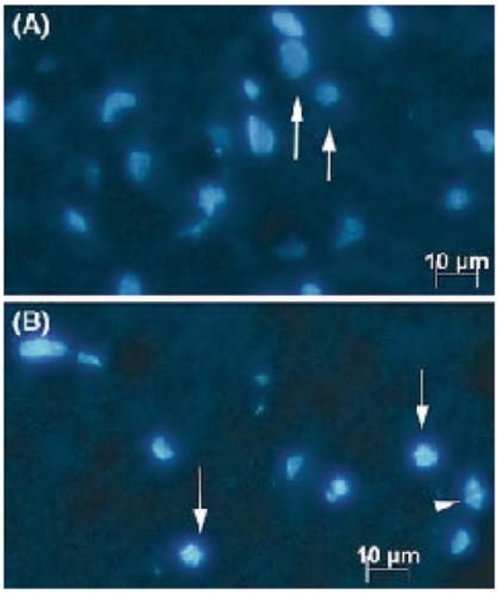


Fig. 10. Hoechst staining in SN following intranigral MPP$^+$ infusion (64 nmol in 1 µl). Representative photomicrographs of SN in the contralateral (**A**) or in the ipsilateral (**B**) side of MPP$^+$ infusion are shown at higher magnifications. The nuclei in the ipsilateral side (**B**) are fluorescing intensely, shrunken in size and irregular in shape (compare nuclei marked with arrows in Fig. 10A with that in Fig. 10B), while some nuclei reveal fragmented DNA (see arrowhead) in contrast to the normal nuclei in the contralateral side (**A**) with smooth margins.

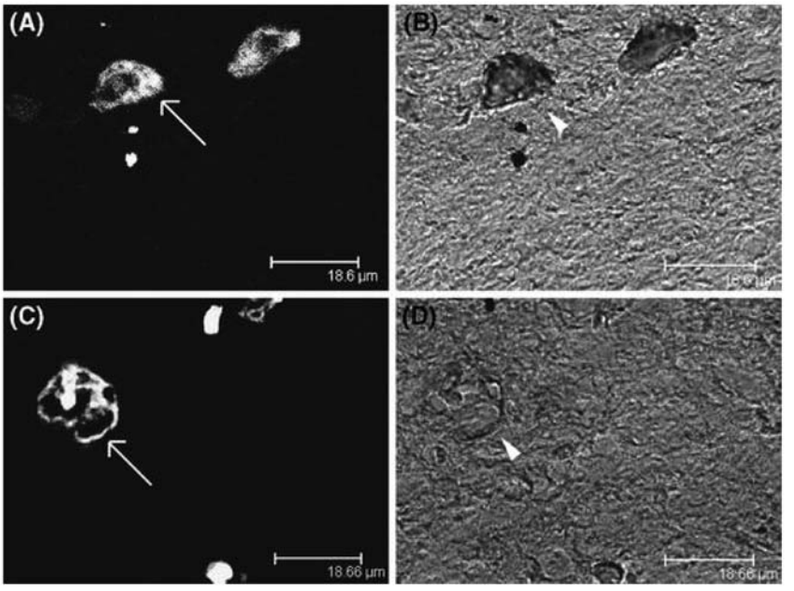


Fig. 11. Acridine orange staining in SN following intranigral MPP$^+$ (64 nmol in 1 µl) infusion. The fixed brains were cut coronally at 5 µm passing through SN (substantia nigra) and stained with acridine orange. Representative photomicrographs of confocal laser images of contralateral SN reveal normal cells [arrow--under bright field; (A), arrowhead--under phase contrast; (B)] with centrally located nucleolus while in the ipsilateral side the representative cell [arrow--under bright field; (C), arrow head--under phase contrast; (D)] shows massive chromatin condensation with a marginally placed nucleolus

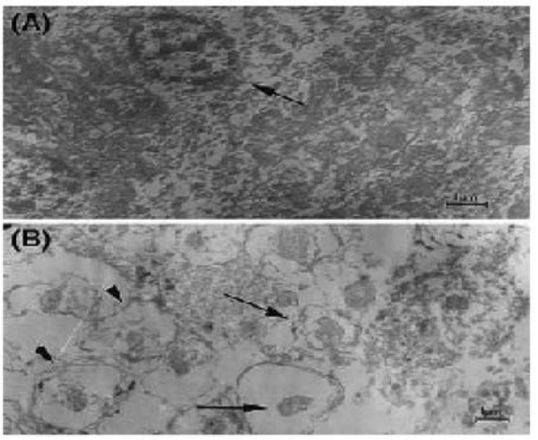


Fig. 12. Ultrastructure micrographs of SN following intranigral MPP^+ infusion. Representative photomicrographs of electron micrographic images of SN contralateral to the side of infusion show a cell with normal nucleus (arrow; A) while shrunken cells (arrowheads; B) with condensed nuclei (arrows; B) are prominently visible in the ipsilateral side of infusion

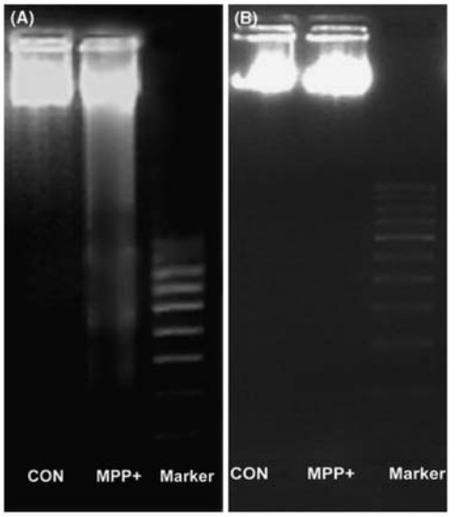


Fig. 13. DNA ladder in nigrostriatal nuclei following to intranigral MPP^+ infusion. Anesthetized animals infused with MPP^+ (64 nmol in 1 µl) were sacrificed on the 5th day following the neurotoxin administration. Substantia nigra (SN; A) and nucleus caudatus putamen (NCP; B) from the treated animals, ipsi- and contralateral to the infused side were micropunched separately. DNA was isolated from these tissues and assayed for fragmentation by electrophoresis on a 2% agarose gel. 10 µg of sample DNA was loaded into each well.

Effect of MPP^+ on cholinergic and dopaminergic neurons

Unilateral intrastriatal infusion of MPP^+ (100 and 200 nmol in 4 µl saline) caused a dose-dependent depletion of striatal DA (69 and 92%, respectively), as measured employing HPLC electrochemistry. It also resulted in the loss of TH immunoreactivity in the striatum and in the perikarya at substantia nigra pars compacta (SNpc) (Fig. 14) and acetylcholinesterase histoenzymological staining in the striatum (Fig. 15). Specific nuclear staining employing Hoechst 33342 (Fig. 16) and acridine orange (Fig. 17) revealed distorted and spindle shaped nuclei, and perinuclear positioning of nucleolus, respectively, for the former and latter dyes in several of the cell populations in the ipsilateral striatum compared to the contralateral side. Existence of a widened lateral ventricle at the side that received the neurotoxin, as well as denser cellular population, as compared to the contralateral side under transmission electron microscope (Fig. 18) evidenced general shrinkage of the striatum. Extensive damage of the nuclei was visible in the cell bodies in the treated side. These results demonstrate non-specific damage extending to the cellular groups including cholinergic neurons in addition to dopaminergic neurons in the striatum to intrastriatal administration of the parkinsonian neurotoxin, MPP^+.

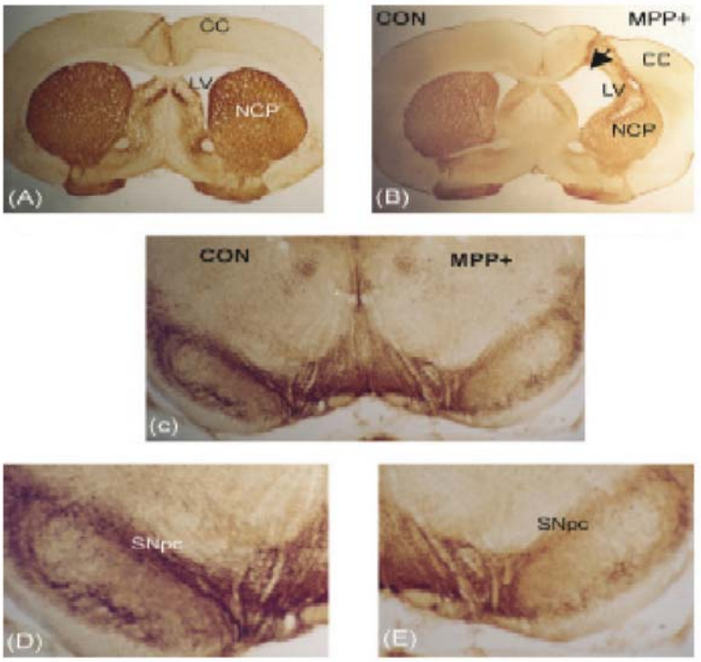


Fig. 14. TH immunoreactive cells in the SN and fibers in NCP, 5 days following unilateral intrastriatal infusion of MPP^+ (100 nmol in 4 µl) or saline. (A) Saline-infused sham control (magnification 12X). (B) Coronal section passing through the striatum from animal that received MPP^+ in the right NCP (magnification 12X). (C) Coronal section passing through SNpc region from animals that received MPP^+ in the right striatum, showing TH staining bilaterally (magnification 16X). (D) Higher magnification (32X) of the left side that shows the SN, contralateral to the side of MPP^+ infusion. (E) Same magnification of the right hand side of 'C', depicting the ipsilateral SN to the side of MPP^+ infusion. CC: cerebral cortex; CON: control; LV: lateral ventricle; NCP: nucleus caudatus putamen; SNpc: substantia nigra pars compacta.

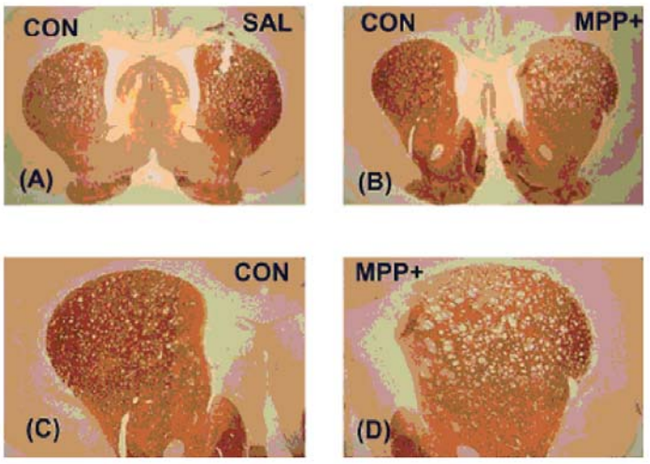


Fig. 15. Acetylcholinesterase histochemistry in NCP, 5 days after infusion of MPP^+. Animals intrastriatally infused with MPP^+ (100 nmol in 4 ml) were perfused with 4% paraformaldehyde on the 5th day. Coronal sections (20 mm) were then taken and processed free floating for the enzyme reaction. Photographs show a representative section showing the NCP from a: (A) saline infused rat (12X) and (B) MPP^+ infused rat (12X). Contralateral (C) and ipsilateral (D) striata are shown magnified (32X).

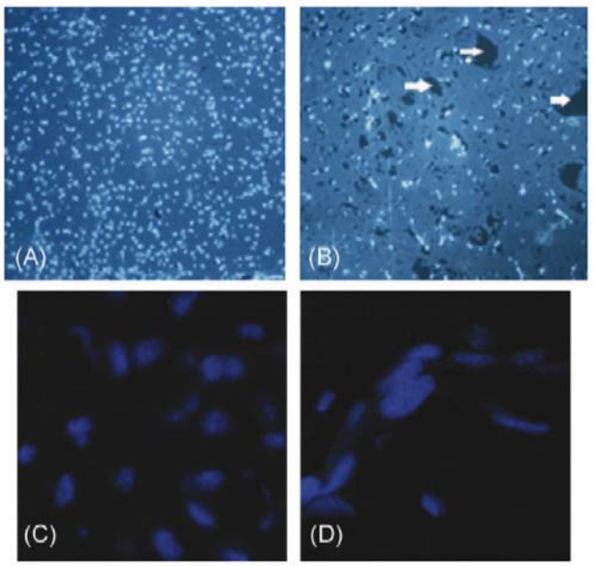


Fig. 16. Nuclear staining with Hoechst 33342 in NCP following intrastriatal MPP^+ infusion. Animals infused intrastriatally with MPP^+ (100 nmol in 4 ml) were perfused with 4% paraformaldehyde on the 5th day. The fixed brains were paraffin embedded and cut coronally at 5 µm passing through nucleus caudatus putamen (NCP) and stained with Hoechst 33342. Representative photomicrographs of NCP in the (A) contralateral and (B) ipsilateral sides of MPP^+ infusion (magnifications 20X; under fluorescence microscope). Arrows indicate tissue damage. Confocal image of NCP region in the contralateral (C) and ipsilateral (D) sides of MPP^+ infusion (magnifications of 1000X).

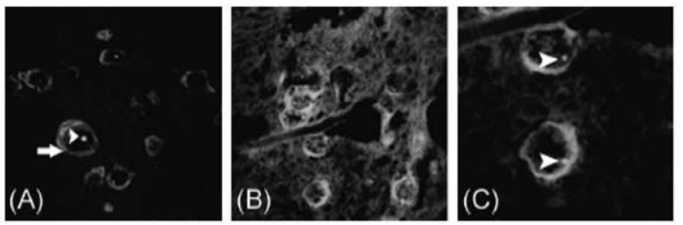


Fig. 17. Acridine orange staining in striatum following intrastriatal MPP^+ infusion. Animals infused intrastriatally with MPP^+ (100 nmol in 4 ml) were perfused with 4% paraformaldehyde on the 5th day. The fixed brains were paraffin embedded and were cut coronally at 5 µm. The sections passing through nucleus caudatus putamen (NCP) were stained with acridine orange. (A) Representative photomicrographs of confocal laser images of NCP contralateral to the side of MPP^+ infusion. Magnification 1000X, zoomed at 1.62. Arrow indicates nucleus and arrowhead indicates nucleolus. (B) Lesioned NCP ipsilateral to the side of MPP^+ infusion at a magnification of 1000X zoomed at 1.87. (C) Higher magnification of 'B', showing two nuclei at 1000X, zoomed at 3.95; arrowheads indicate nucleoli.

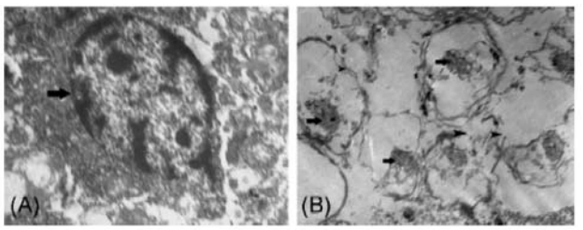


Fig. 18. Transmission electron micrograph after neurotoxin exposure. (A) Control side; **(B)** treated side. Arrow in **(A)** intact nucleus. Arrows in **(B)** show shrunkon nuclei. Arrowheads midicated shrunken cells.

Melatonin in rotenone-induced Parkinsonism

Work from others and our laboratory established that rotenone, a well-known pesticide and mitochondrial complex-I inhibitor, produces behavioural, neurochemical and neuropathological symptoms akin to PD. The hemiparkinsonian animals showed drug-induced stereotypic rotations, striatal dopamine (DA) depletion and loss of tyrosine hydroxylase (TH) positive neurons in DA-ergic cell body region, substantia nigra pars compacta (SNpc). Our study has shown the neuroprotective effects of melatonin - a potent antioxidant, against rotenone-induced neurotoxicity. The most important observations made herein are: (i) significant reduction of the rotenone-induced •OH formation (Fig. 19) in the mitochondria by melatonin (ii) a total reversal of rotenone-induced GSH depletion (Fig. 20) following chronic doses of melatonin, (ii) significant upregulation of the activity of SOD (Fig. 21A) following acute doses of melatonin, and further activation in the rotenone-damaged SN, and (iii) melatonin-induced enhancement in the activity of catalase (Fig. 21B) in the affected SN.

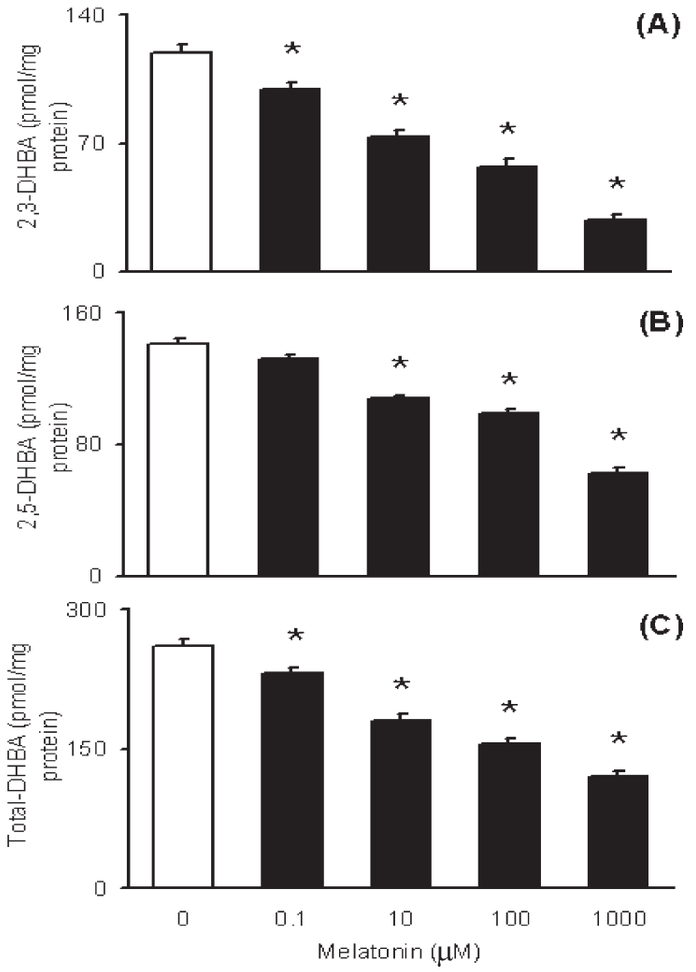


Fig. 19. Effect of melatonin on rotenone-induced •OH generation in the mitochondria. Mitochondrial P2 fractions from rat were incubated with rotenone (100 μM) for 30 min in the absence or presence of melatonin (10^{-7}-10^{-3}M). •OH adducts of salicylate, 2,3- and 2,5-dihydroxy benzoic acid (DHBA) formed were measured by employing a sensitive HPLC electrochemical detection method. (A) 2,3-DHBA levels, (B) 2,5-DHBA levels, (C) total DHBA levels. Data are expressed as pmol/mg protein.

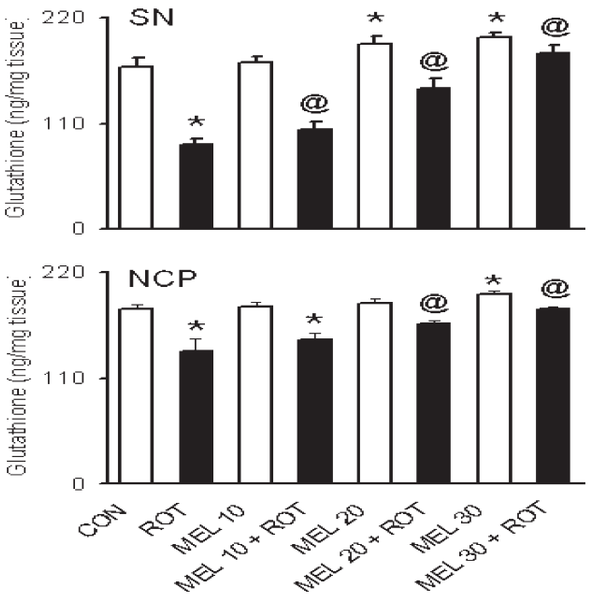


Fig. 20. Effect of melatonin on rotenone-induced glutathione (GSH) depletion in substantia nigra (SN) and nucleus caudatus putamen (NCP). Adult male Sprague-Dawley rats, intranigrally infused with rotenone (6 g in 1 L) were administered vehicle or melatonin (10, 20 and 30 mg/kg; i.p.) at 12-hr intervals for 4 days. Animals were sacrificed on the fifth day. Contra and ipsilateral SN and NCP were dissected out and analyzed for GSH levels by a sensitive spectrofluorimetric procedure. There existed no significant change between vehicle-infused SN or the SN which was left intact. Data are expressed as ng/mg tissue.

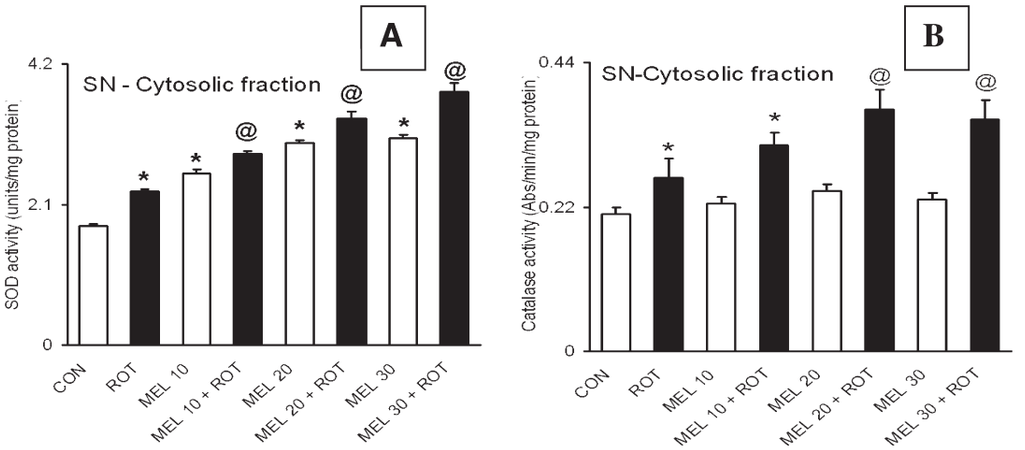


Fig. 21. Effect of melatonin on rotenone-induced changes in superoxide dismutase (SOD) activity (A) and catalase activity (B). Adult male Sprague-Dawley rats, intranigrally infused with rotenone (6 µg in 1 µL) were administered vehicle or melatonin (10, 20 and 30 mg/kg; i.p.) at 12-h intervals for 4 days. Animals were sacrificed on the fifth day. Contra- and ipsilateral substantia nigra (SN) were dissected out and cytosolic fractions were analyzed for SOD and catalase activity. One unit of the enzyme for SOD activity is defined as 50% inhibition/min/mg protein The catalase activity was analyzed by monitoring the disappearance of hydrogen peroxide in presence of the enzyme in cytosolic fraction prepared from SN. Specific activity of the catalase enzyme is described as change in absorbance at 240 nm/min/mg protein.

Dr. Sumantra Das and group

Structure, function and altered function of astroglial cells

Our earlier studies on the signal transduction pathways associated with thyroid hormone (TH) induced differentiation and maturation of astrocytes had identified a profound role of the ß-adrenergic receptor (β-AR) system as a downstream regulator of the hormonal action. We, therefore, investigated the effect of TH on the β-AR subtypes. Radioligand binding studies using ^{125}I-pindolol (^{125}I-PIN) in absence and presence of specific

β_1- and β_2-AR antagonists showed a gradual increase in the specific binding of β_2-AR when observed at 5 days, 10 days, 15 days and 20 days in astrocytes cultured, both in absence and presence of TH. At all ages of culture, TH caused an increase in binding of ^{125}I-PIN to β_2-AR compared to TH-deficient controls. There was a significant increase in the affinity of the receptors (Kd) in the TH-treated cells without any change in receptor number (Bmax). β_2-AR mRNA levels, measured by real-time PCR at various times starting from 2 h to 24 h, however, did not show any significant changes during TH treatment as compared to untreated control and confirmed that increased binding of ^{125}I-PIN to β_2-AR was not due to increase in receptor number. This prompted us to investigate the role of other regulators of β-AR system. Western blot analysis demonstrated that at early time point between 2 h to 12 h, addition of TH to astrocyte cultures grown under hypothyroid conditions caused a gradual decline in phospho ß-Arrestin levels which came back to basal level by 24 h (Fig. 22). Result suggests a possible involvement of β-Arrestin in modulating the increased affinity of β_2-AR in astrocytes exposed to TH.

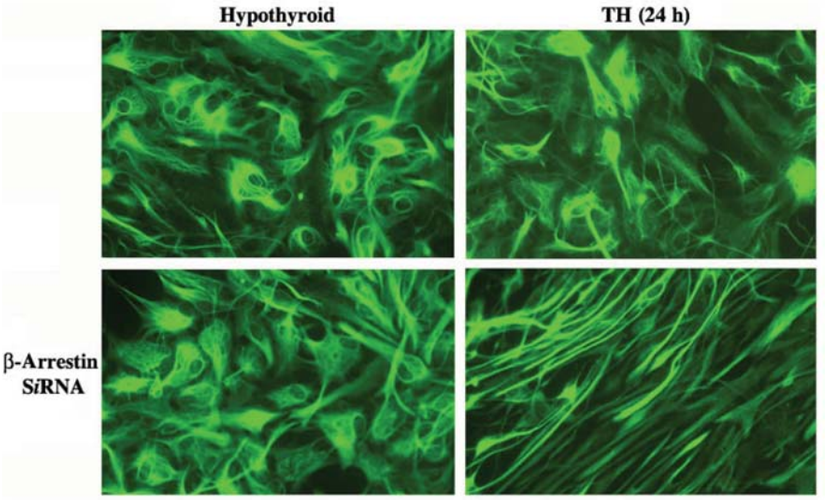


Fig. 22. TH decreases phospho β-arrestin activity in 10-day old primary astrocyte culture: A rapid fall by 2 h with a peak decline at 6 h which comes back to basal level by 24 h.

Hypothyroidism in the developing rat brain is associated with enhanced oxidative stress, one of the earliest manifestations of which is a decline in the level of glutathione (GSH). A collaborative work has been undertaken to investigate the role of TH on the activity of glutamate cysteine ligase (GCL), previously known as gamma-glutamyl synthetase (γ-GCS). Hypothyroidism in developing rat brain declined the activity of GCL. Conversely, administration of TH to hypothyroid rats elicited an increase in the activity of the enzyme. TH treatment of astrocytes resulted in a rapid increase in the level of GSH and this up-regulation was completely inhibited by L-buthionine S, R-sulfoximine (BSO). Quantitative RT-PCR analysis revealed that astrocytes contained a basal excess of GCLC (catalytic subunit of GCL) mRNA, relative to GCLM (modulator subunit of GCL) mRNA, the ratio being 4:1. TH treatment led to a differential increase in the expression of these two mRNAs, which resulted in a decline in the stoichiometric ratio of GCLC:GCLM mRNA that may favor holoenzyme formation with enhanced catalytic efficiency. TH treatment improved the antioxidative defense in astrocytes by enhancing their hydrogen peroxide scavenging ability with a decrease in peroxide half-life (Fig. 23).

The overall results suggest that TH plays a positive role in maintaining GSH homeostasis in astrocytes and in protecting the brain from oxidative stress.

In a recent study, we have observed a protective role of TH against loss of cell viability of cultured astrocytes when exposed to chronic morphine. Decline in cell viability on exposure to morphine has been shown to be due to programmed cell death as confirmed by DNA fragmentation assay (TUNEL) and annexin-PI staining (Fig. 24).

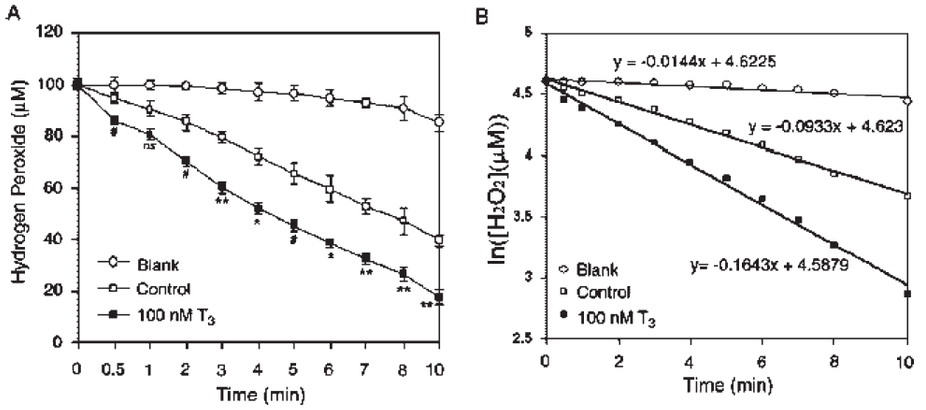


Fig. 23. Effect of TH on the clearance of H_2O_2 from the minimal media of astrocyte primary cultures. (A) Astrocyte cultures (12 days old) were pretreated without (Control) or with 100 nM T3 for 24 h. After a subsequent preconditioning of the astrocytes for 5 min at 37°C in minimal media, the cells were treated with 100 μM H_2O_2 for 10 min and the peroxide remaining in the media was determined from aliquots withdrawn at indicated time points from each dish and plotted against time. Values represent mean ± SE of four determinations from independent sets of astrocyte culture. ns, difference not significant. Significant differences relative to untreated control are indicated as: # $P < 0.05$; * $P < 0.01$; ** $P < 0.005$. (B) Semilogarithmic representation of the peroxide concentration against time [data shown in (A)]. Half-lives of H_2O_2 determined from slopes of regression lines of the semilogarithmic plot were 7.4 min for control dishes with untreated astrocytes and 4.2 min for dishes with astrocytes that been pretreated with 100 nM T3 for 24 h. Blank plates containing minimal media with 100 μM H_2O_2 without astrocytes showed a peroxide halflife of 48.1 min under identical conditions.

Supplementation of TH to media prevents the apoptosis. Morphine induced apoptosis is mediated through the opioid receptors since the opioid receptor antagonist, naloxone attenuates morphine action. nNOS, producing NO, plays as a key regulator of morphine induced cell death, as 7NI, a nNOS inhibitor completely blocks the loss of viable cells. Further studies suggest that the protective role of TH, is not due to the enhancement of glycolytic pathway in astrocytes during the high level of NO exposure, which protects astrocytes from NO induced mitochondrial membrane dysfunction, because inhibition of AMP kinase, one of the controlling factor of glycolytic enhancement whose level of expression is influenced by TH, did not attenuate TH function. On the other hand, the glutathione synthesizing inhibitor, BSO antagonized the protective role of TH. GSH is the major free radical scavenger in cells and its level was found to decline in astrocytes cultured under TH-deficient conditions. Further studies on the signal transduction pathway involved in morphine induced cytotoxicity suggest peroxinitrite, -ONOO-induced decline in levels of both pMAPK and pAKT, the two well known factors involved in cell survival.

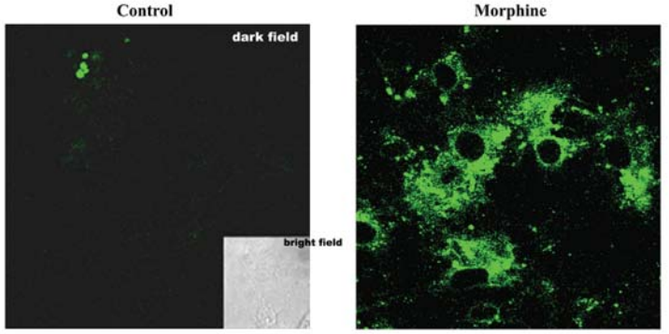


Fig. 24. Morphine causing apoptosis in astrocytes in primary cultures. Coverslip cultures of 10-day old astroglial cells were processed for immunofluorescence staining with Annexin V-FITC and viewed under confocal spectral microscope. Annexin V binds with phosphatidyl serine, which is expressed on cell surface during apoptosis.

We have previously reported that the omega-3 polyunsaturated fatty acid, docosahexaenoic acid (DHA, 22:6n-3), plays a unique role in facilitating some of the vital functions of astrocytes in the developing brain. DHA is synthesized in the mammalian brain from the dietary intake of its precursor, α-linolenic acid (ALA, 18:3n-3), in the form of oils. The choice of fats and oils vary considerably amongst population in India. So also does the FA composition of each source of oils and fats. In view of our previous observations, such varied dietary intake of oils envisages a closer look at the role of these in the development and function of astroglial cells.

FAs were isolated from commonly used oils in diet like sunflower oil, soyabean oil, mustard oil, coconut oil, safflower oil, rapeseed oil and linseed oil and their composition were determined by GLC. Immunoflourescence studies of astrocyte cultures supplemented with 100 ng of FAs, isolated from each oil demonstrated variations in morphology. β-AR binding was increased in case of mustard, soyabean and linseed oils. In Indian style of cooking, oils are exposed to high temperatures whereby the *cis* double bonds of PUFA are converted to *trans* and peroxised forms. Hence parallel studies were conducted with fatty acids from oils, which were heated for 72 hours. GLC analysis showed there is a decrease in total unsaturation levels while saturated fatty acid increases. Only mustard and linseed oils contain ALA, which is present in both the raw and heated forms. The levels of ALA were less in the heated forms. The morphology of astrocytes supplemented with FAs from heated oils were considerably different from astrocytes supplementd with FAs from raw oils. The β-AR binding results show that there is a decrease in binding of astrocytes supplemented with FAs from heated oils. The expression of GFAP also changes in astrocytes supplemented with FAs from different oils and their heated counterparts (Fig 25). Overall, the effects of various commonly used oils on astrocyte structure and function have been reviewed.

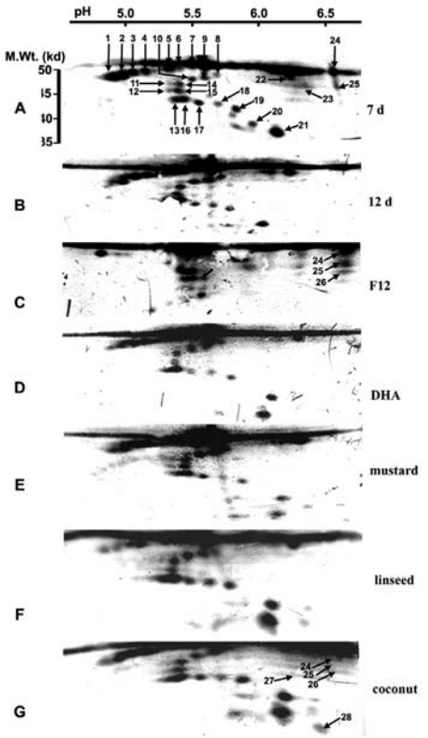


Fig. 25. Effect of supplementation of fatty acids isolated from oils on the expression of isoforms of GFAP by 2D electrophoresis. Astrocytes cultured under various treatment conditions were subjected to 2D electrophoresis followed by western blotting with GFAP. Details of the methods are described in Methods. Figures are representative of atleast 3 experiments. A, B represents immunoblots of astrocytes cultured for 7 and 12 days respectively in normal serum. Astrocytes were cultured in serum free medium (C), or in medium supplemented 100 nM DHA (D), 100 ng of FAs isolated from mustard oil(E), linseed oil (F) and coconut oil (G) dissolved in 0.1% ethanol for an additional 2 days.

Newer approaches for the treatment of narcotic addiction

A series of substituted quinolines, synthesized by the Syntheic, Biophysical and Natural Product Chemistry group, have been found to have significant interaction at the μ-opioid receptor. A few of these also have activity at the κ-opioid receptor. Two such compounds have been tested and found to antagonize naloxone precipitated withdrawal in morphine dependent mice. Further work is in progress to evaluate the potential of these compounds in addicted models.

Another collaborative project with a psychiatric clinic, Baulmon, Kolkata has been undertaken to carry out genetic epidemiological studies on opioid addiction by investigating the possible correlation of specific SNPs of certain candidate genes like μ-opioid receptor, κ- opioid receptor etc. with any feature of addiction. DNA samples of normal, opioid addicts with or without relapse were subjected to PCR based RFLP which was supported by DNA sequencing analysis.

Limbal stem cell culture

A collaborative project with Regional Institute of Ophthalmology, Kolkata has been initiated with the purpose of reconstructing damaged cornea in ocular surface disorders by transplantation of corneal epithelium from cultured limbal stem cells (Fig. 26).

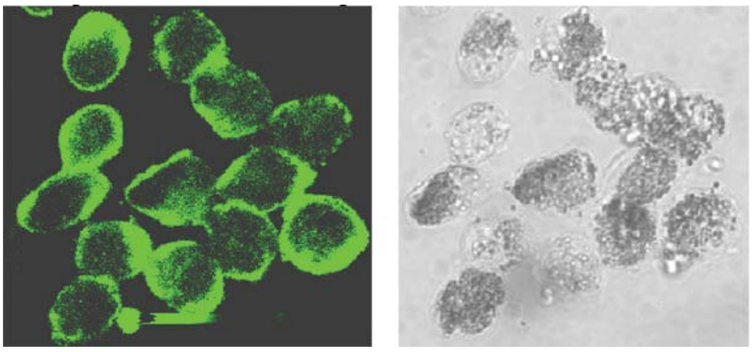


Fig. 26. Positive immunofluorescence staining of cultured limbal epithelial cells with Integrin β (Left panel). Corresponding bright field photomicrograph is shown in right panel. Cadaver eyes from regional eye bank were used for establishing primary cell culture.

REPRODUCTIVE BIOLOGY

Dr. Sandhaya R. Dungdung and group

Biochemical basis of the regulation of sperm motility

Blood serum of goat has been shown to possess an activity that markedly stimulated goat cauda epididymal sperm forward motility. Serum applied at a range of 2 - 8 % (v/v) increased sperm forward motility to the extent of 30 - 150 %, on microscopic assay. Further increase of serum concentration [12% (v/v) or above] caused gradual reduction in forward motility. Spectrophotometric assay showed about 25% increase in forward motility on application of 4% (v/v) serum. At present work is in progress for the purification of this motility stimulating protein that may have an important role in the regulation of mammalian sperm motility.

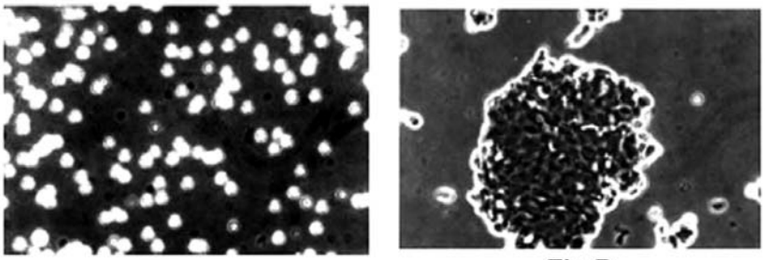


Fig. A Fig. B

Fig. 27. Agglutination of Rabbit erythrocytes with highly purified isolated sperm plasma membrane. Erythrocytes were isolated and agglutination studies were carried out. (A) Untreated erythrocytes (control), (B) Control cells + extracted sperm membrane (0.2 mg protein/ml).

We found a lectin-like molecule located on the sperm surface specifically interacts with its receptor of the neighboring homologous cells to cause autoagglutination. Fig. 27 represents rabbit erythrocytes agglutination after treatment with highly purified sperm plasma membrane. Failure of the pre- and post-distal corpus sperm to show autoagglutination is due to lack of lectin-like molecule and its receptors, respectively. Maturing sperm at distal-corpus stage acquire the lectin-like molecule followed by sharp disappearance of its receptor and this event is synchronously associated with the initiation of sperm forward motility that is essential for fertilization in vivo. The purification and characterization of lectin and its receptor from goat epididymal spermatozoa is under progress.

Dr. S. N. Kabir and group

Physiological and pathophysiological aspects of female reproduction premature ovarian failure

Premature ovarian failure (POF) is a heterogeneous entity for which the etiological bases or pathophysiologic mechanisms are largely unknown. We have demonstrated that experimental attenuation of embryonic galactosyltransferase inhibits germ cell migration and leads to development of ovary with deficient follicular reserve that characterizes basic tenets of POF and may serve as a model for the disease. Using this model, it was evident that the number of follicles in the ovarian reserve impacts the rate of follicular atresia. The low the follicular reserve, the greater the rate of apoptosis, which was evidenced by increased granulosa cell caspase activity and DNA fragmentation (Fig. 28). Transplantation of neonatal ovary beneath the bursa of the follicle-deficient ovary could reverse ovarian function and induce advancement of puberty. The findings taken together suggest that as the number of follicles wane below, either as a part of aging process, or as a consequence of chemical or mechanical trauma, the rate of apoptosis in the residual pool increases, which triggers accelerated follicular loss and advancement of ovarian failure. Thus the number of follicles in the ovarian pool possibly plays determining roles in their battle for own survival, and declining follicular reserve is perhaps one of the thrusts that increases the rate of follicular depletion during the final phase of ovarian life.

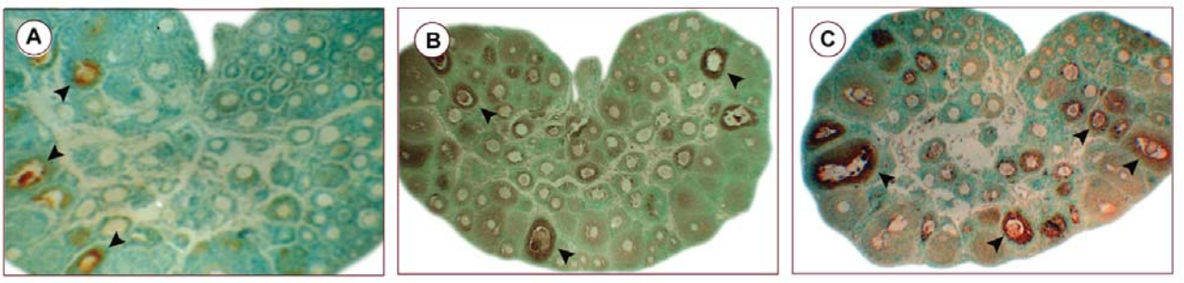


Fig. 28. Immunohistochemical localization of nuclei with fragmented DNA by TUNEL reaction. Note increased rate of follicular atresia in the GalTase-attenuated rat ovaries (B & C) as compared to control (A).

Search for spermicidal principles of plant origin

Except male condom, practically no prophylactic device is available for protection against pregnancy as well as heterosexual transmission of HIV infection. Attention has therefore been focused on development of topical microbicides (vaginal or rectal products that would interfere with HIV infection) with discerning spermicidal property, especially for formulations that may be available over the counter. The objective is to get dual protection: protection against unplanned pregnancy, and protection against HIV infection.

Ac-B, a lead molecule with spermicidal potential, was tested for anti-HIV property *in vitro*. HIV was treated with or without Ac-B. Cells were infected with the treated or untreated virus and cultured in the presence or absence of Ac-B. Virus production was analyzed by P24 antigen ELISA at term.

Cells infected with Ac-B-treated HIV and cultured in the presence of Ac-B showed complete inhibition of HIV transmission and replication at concentrations significantly below its cytotoxic level (>2.5 mcg/ml). Partial inhibition was noted when the cells were infected with treated HIV but cultured in the absence of Ac-B (Fig. 29). Cells infected with untreated virus but cultured in the presence of Ac-B exhibited no inhibition of HIV replication. This observation clearly indicates that Ac-B has anti-HIV activity and highlights the credential of Ac-B as a prospective candidate for future development of spermicidal microbicide.

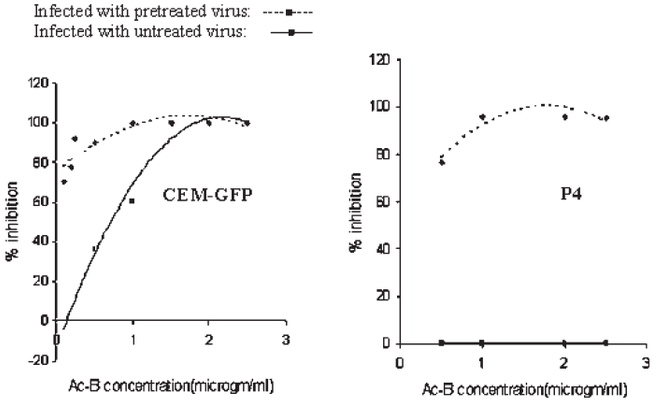


Fig. 29. HIV replication in CEM-GFP and P4 cell lines.

Microbicides/spermicides are products meant for topical (vaginal/rectal) administration that mostly exposes vaginal/rectal wall and surface of the penile glans directly to the contact of the agent. The agents may get absorbed through these routes and reach the systemic circulation across leading to local as well as systemic effects. From the safety point of view, we therefore conducted a battery of tests for tolerance of the target organs to Ac-B and prima facie toxicity.

Haemoglobin release from RBC is an excellent end-point for study of cell membrane integrity. Haemolytic index (concentration required for 50% hemolysis of RBCs), which is used as a rapid screening assay of first-order for the assessment of acute irritation potential leading to toxicity, for Ac-B was found to be 7 mcg/ml. Since a clinical formulation is yet to be prepared, for topical application a galenic formulation was made with K-Y Jelly (i.e. a non-toxic, inert lubricant jelly which is widely used in human as well as animals) in doses of Ac-B ranging from 10^3 - 10^5 folds of haemolytic index (i.e. 7 mg, 70 mg and 700 mg/ml), while water-based solution at 7 mg, 70 mg and 700 mg/kg body weight was used for systemic administration. The work is in progress.

Dr. Smritinath Chakraborty and group

Search for fertility regulating agent/s from natural resources and/synthetic origin

Previously contragestational effect was reported of n-butanolic fraction of the aqueous extracts of *Chenopodium album* seeds. The effect was associated with significant decline in peripheral progesterone level. Exogenous administration of HCG was unable to protect the pregnancy of the extract treated rats. Progesterones reversed the effects, so it may be stated that the effect is not primarily due to the pituitary deficiency. Some other causes such as disturbance in the delicate balance of estrogen/progesterone could be the effective cause. Work are in progress to specify the mechanism of action and also to isolate the specific active principle. In another attempt alcoholic extract of the root of the medicinal plant *Sesbania sesban* Merril has been tested for fertility regulating potential with an aim to isolate non-steroidal antifertility principal from plant. The extract showed significant anti-implantation, also spermicidal activities. Attempt was taken to fractionate the crude extract chromatographically. Besides in a collaborative study some indole derivatives were assessed for their anti spermatogenic potency. One of the compounds was found to reduce functional fertility in male rats. Measurement of the hormones and the biochemical parameters are in progress.

Biocompatibility study of ceramic-polymer composites as replacement of bone, skin graft etc.

In health care management repair of bony hard tissue is a major challenge and in many cases ends of the bones cannot reunite which is more problematic. Local defects in bone arising as a result of trauma, tumor, infection etc could frequently be restored by graft substitutes. Earlier we have developed a reliable method of bone replacement material composed of alumina reinforced ultra high molecular weight polyethylene composite. Surface of the material was deposited with bioactive coating [hydroxyapatite or bio glass] for better attachment of the muscles, improve the osso-integration and to achieve adequate fixation with bone. It would be better than steel as replacement material for bone. Physical characteristics such as surface topography, roughness, porosity, coating thickness and load bearing capacity etc were examined using different tests system. The material was found to be ideal to mimic micro architecture of the bone. Bioactivity and "tissue bonding" of the material with coating was characterized on in-vivo experiment, implanting the material in rat thigh muscle. Both SEM and microscopic studies revealed that the tissue attachment was normal, showing no deformities of muscles and other soft tissues around the composite strip. Besides, cells can adhere without particular problem/s to such foreign material and adhesion takes from development of a proteinaceous film upon which cell colonies rooted. The bond was strong enough with such hydroxyapatite or bio-glass coating. Normal tissue regeneration was also noticed. Hard tissue attachment was also examined after three months of implantation of the material on hole made on hipbones of rats. The attachment was strong and osteoconductive, indicated biocompatibility of the polymer-composite.

Hipbone prosthesis [femur with trochliear head] was successfully constructed using the polymer- composite coated with the same compositions. All the physical properties including load bearing capacities were tested, then the prosthesis was surgically implanted/ fitted to rabbit's pelvic-girdle which is working perfectly for the last one year without symptoms. We are interested in large-scale repeat, observation in rabbit and also if possible in some other higher animals.

Adverse impacts of statin on reproductive functions

Dr. Padma Das and group

Statins are a group of drugs that are routinely advised to reduce the cardiovascular risks associated with hypercholesterolemia. Statin acts through the inhibition of HMG-CoA reductase leading to termination of cholesterol biosynthesis with the production of HMG-CoA and reduced cholesterol synthesis. On the other hand,

cholesterol is the basic building block of steroidogenesis. Sex steroids play crucial roles in almost all aspects of normal reproductive functions. In pregnancy the demand of sex hormone production increases further by several hundred folds. Therefore, a severe insult on steroidogenesis is likely to have adverse impacts on steroidogenesis. The objective of this study was to evaluate the effects of different statin on the course and outcome of pregnancy.

Pregnant rats were given vehicle (1 ml), Pravastatin, Atorvastatin or Simvastatin by oral gavage at 3 different dose levels, 10 mg/ml, 20 mg/ml or 40 mg/ml per rat, during days 5-15 of pregnancy. We have demonstrated that Pravastatin at the dose level of 10 mg/ml and Atorvastatin up to the dose level of 20 mg/ml exerted no adverse impact on the course and outcome of pregnancy, as compared with that of control. But a significant reduction in the number of live foetus was evident in the groups treated with Atorvastatin at 40 mg/ml. Simvastatin, on the other hand exhibited interceptive effects at all dose levels. The number of sites reduced significantly in a dose-dependent manner. At 40 mg/ml dose levels, Simvastatin exerted cent percent interceptive effects leading to loss of all implantation sites, and producing no live or dead embryo. The preliminary study shows that statins are embryotoxic at higher doses. Use of statin may therefore be contraindicated in pregnancy. To unveil this mode of action, the work on precise mechanism of embryotoxic effects of statin are in progress.

Studies on the antifertility effects of Sesbania grandiflora

Sesbania grandiflora flowers and leaves extracts are being tested for their antifertility effect in Sprague Dawley rats. Results are yet to be obtained and work will continue.

Names of Technical Staff

Mr. Herambananda Ray, Dr. Shampa Sarkar, Mr. Swapan Kumar Mandal, Mr. Prabir Kumar Dey, Mr. Shyam Sundar Nandi, Mr. P. C. Deuri

Names of RAs, Pool Officers, SRFs and JRFs

Dr. Anindita Joardar, Dr. Kakali De, Dr. Tanima Kundu, Dr. Navneet AK, Dr. Sonali Ghosh, Asmita Dasgupta, Pamela Ghosh, Ishani Deb, Mritunjay Pandey, Merina Varghese, Debabrata Biswas, Reena Haobam, Mausam Ghosh, Sreetama Sen, Tathagata Sengupta, Sudipa Saha Roy, Kaustav Dutta Chowdhury, Dijendra Nath Roy, Sreerupa Ghose Roy, Priyanka Dey, Sumita Mishra, Sangeeta Maity, Vivek Chander, Samir Kumar Saha, Debleena Dey, Deepak Kumar, Pomy Barma, Debanjali Mitra, Goutam Chandra, Anupom Borah, Ambili Appukuttan, Poornima Chandran, Kaushik Das, Sudipta Saha, Sandip Bag.

Summer Trainee

Sangeeta Hareendran

Molecular & Human Genetics

Dr. Samit Adhya, Dr. Keya Chaudhury, Dr. Kunal Ray, Dr. Ashok Kumar Giri, Dr. Susanta Roychaudhury, Dr. Samir Kumar Dutta

The broad aims of the division are to understand the molecular genetic basis of diseases common in Indian populations, to study gene expression and function in pathogenic microorganisms, and to develop transgenic plants with improved characteristics.

The specific objectives are : to decipher the molecular basis of the genomic instabilities in head and neck cancer (HNSCC) and to identify the putative tumor suppressor genes involved in the development of this cancer: to identify susceptibility alleles in *Helicobacter pylori* associated gastroduodenal diseases; to study the molecular pathogenesis of oral submucous fibrosis; to understand the molecular genetics of haemophilia, glaucoma, Wilson disease, and oculo-cutaneous albinism; to assess the health effects, genetic damage and genetic variants in populations exposed to arsenic through drinking water in West Bengal; to test the antimutagenic and anicarcinogenic effects of black tea polyphenols theaflavins and thearubigins; to identify differentially expressed *V. cholerae* genes following infection to host and their role in pathogenesis, and to study the response of human intestinal epithelial cells to *V. cholerae* infection; to study the molecular basis of the import of nuclear-encoded tRNAs into the mitochondria of the kinetoplastid protozoon *Leishmania* using a combination of biochemical and reverse genetic approaches; to identify, isolate and modify genes from non-host plants involved in self-defence mechanisms against pests; and to transfer them as bio-pesticides to host plants.

A new Leishmania mitochondrial tRNA import receptor

Dr. S. Adhya and group

Transport of tRNAs across the inner mitochondrial membrane of the kinetoplastid protozoon *Leishmania* requires interactions with specific binding proteins (receptors) in a multi-subunit complex. The allosteric model of import regulation proposes cooperative and antagonistic interactions between two or more receptors with binding specificities for distinct tRNA families (Type I and Type II respectively). To identify the Type II receptor, the gene encoding RIC8A, a subunit of the complex, was cloned. The C-terminal region of RIC8A is homologous to subunit 6b of ubiquinol cytochrome c reductase (respiratory complex III), but the protozoal protein has intrinsic affinity for Type II, but not for Type I, tRNAs. RIC8A/UCR6b is shared by the import complex and complex III, indicating its bi-functionality, but is assembled differently in the two complexes. Knockdown of RIC8A/UCR6b in *Leishmania* lowered the mitochondrial content of Type II tRNAs, but raised that of Type I tRNAs, with downstream effects on mitochondrial translation and respiration, and cell death. In RIC8A/UCR6b-knockdown cells, a sub-complex was formed that interacted with Type I tRNA, but the negative regulation by Type II tRNA was lost. Mitochondrial extracts from these cells were defective for Type II, but not Type I, import; Type II import as well as regulation were restored by purified RIC8A/UCR6b. These results provide evidence for the relevance of allosteric regulation *in vivo*, and indicate that acquisition of new tRNA binding domains by ancient respiratory components have played a key role in the evolution of mitochondrial tRNA import.

Leishmania tRNA import receptor RIC1 is a tRNA dependent ATPase : Transport of tRNAs across the inner mitochondrial membrane of the kinetoplastid protozoon *Leishmania* requires interactions with specific binding proteins (receptors) in a multi-subunit complex. The allosteric model of import regulation proposes cooperative and antagonistic interactions between two or more receptors with binding specificities for distinct tRNA families (Type I and Type II respectively). To identify the Type II receptor, the gene encoding RIC8A, a subunit of the complex, was cloned. The C-terminal region of RIC8A is homologous to subunit 6b of ubiquinol cytochrome c reductase (respiratory complex III), but the protozoal protein has intrinsic affinity for Type II, but not for Type I, tRNAs. RIC8A/UCR6b is shared by the import complex and complex III, indicating its bi-functionality, but is assembled differently in the two complexes. Knockdown of RIC8A/UCR6b in *Leishmania* lowered the mitochondrial content of Type II tRNAs, but raised that of Type I tRNAs, with downstream effects on mitochondrial translation and respiration, and cell death. In RIC8A/UCR6b-knockdown cells, a sub-complex was formed that interacted with Type I tRNA, but the negative regulation by Type II tRNA was lost. Mitochondrial extracts from these cells were defective for Type II, but not Type I, import; Type II import as well as regulation were restored by purified RIC8A/UCR6b. These results provide evidence for the relevance of allosteric regulation *in vivo*, and indicate that acquisition of new tRNA binding domains by ancient respiratory components have played a key role in the evolution of mitochondrial tRNA import.

Functional Delivery of a Cytosolic tRNA into Mutant Mitochondria of Human Cells : Many maternally inherited and incurable neuromyopathies are caused by mutations in mitochondrial (mt) tRNA genes. Kinetoplastid protozoa including *Leishmania* have evolved specialized systems for importing nucleus-encoded tRNAs into mitochondria. We found that the *Leishmania* RNA Import Complex (RIC) could enter human cells by a caveolin-1 dependent pathway, where it induced import of endogenous cytosolic tRNAs including $tRNA^{Lys}$, and restored mitochondrial function in a cybrid harboring a mutant mt $tRNA^{Lys}$ gene. The use of protein complexes to modulate mitochondrial function may help in the management of such genetic disorders.

Molecular analysis of human diseases

Dr. Keya Chowdhury and group

Host-Vibrio cholerae interaction: Transcriptional upregulation of inflammatory cytokines in human intestinal epithelial cells following *Vibrio cholerae* infection. Coordinated expression and upregulation of IL-1α, IL-1β, TNF-α, IL-6, GM-CSF, IL-8, MCP-1 and ENA-78, with chemoattractant and proinflammatory properties belonging to varied cytokine families, were obtained in the intestinal epithelial cell line Int407 upon *V. cholerae* infection. These proinflammatory cytokines also showed increased expression in T84 except IL-6, while a striking dis-similarity in cytokine expression was observed in Caco-2. Gene expression studies of MCP-1, GM-CSF, IL-1α and IL-6 and anti-inflammatory cytokine TGF-α in Int407 cells with *V. cholerae* culture supernatant, cholera toxin (CT), lipopolysaccharide (LPS) and *ctx*A mutant demonstrated that apart from CT and LPS, *V. cholerae* culture supernatant harbors strong inducer(s) of IL-6 and MCP-1 and moderate inducer(s) of IL-1α and GM-CSF. CT or LPS induced cytokine expression is facilitated by activation of NF-κB (p65 and p50) and CREB in Int407. Studies with ctxA mutants of *V. cholerae* revealed that the mutant activates the p65 of NF-κB and CREB and as such the activation is mediated by CT-independent factors as well. We conclude that *V. cholerae* elicits a proinflammatory response in Int407 that is mediated by activation of NF-κB and CREB by CT, LPS and/or other secreted products of *V. cholerae*. Flagellin of *Vibrio cholerae* stimulates IL-1β in human intestinal epithelial cell line Int407 through TLR5 mediated pathway. *Vibrio cholerae*, a noninvasive enteric bacterium and causative agent of the diarrheal disease cholera, induces the secretion of proinflamammatory cytokines including IL-1α; in Int407. Live *V. cholerae* induced IL-1α mRNA expression as early as 2h of infection in Int407, reached a peak at 3.5h and declined thereafter. Kinetics of secretion paralleled IL-1β mRNA expression. The present study investigated the identity of the effector molecule(s), which is largely unknown.

The bacterial culture supernatant showed IL-1β stimulating activity, which was unaltered upon heat treatment but declined with proteinase treatment suggesting the involvement of flagella as an inducer. The aflagellate *V. cholerae* flaA mutant (O395FLAN) resulted in highly reduced level of IL-1β expression in Int407. The flagellin of *V. cholerae* induced IL-1α expression in Int407. Infection of Toll-like receptor5 (TLR5) transfected HeLa cells with O395FLAN showed reduced level of IL-1β mRNA as well as secretion compared to wild type. Unlike wild-type *V. cholerae*, O395FLAN did not activate the NF-κB but *V. cholerae* as well as the recombinant flagellin activates NF-κB, p38 and ERK MAP kinase, which was accompanied by, increased expression and secretion of IL-1β. Our data clearly indicate that flagellin of *V. cholerae* could induce IL-1β expression by recognizing TLR5 that activate NF-κB and MAP kinase in Int407.

Reduction of sodium arsenite induced toxicity by aqueous garlic extract. Arsenic has emerged rapidly as a major pollutant of drinking water in several districts of West Bengal, India, Bangladesh, Taiwan and several other countries. Despite arsenic being a health hazard and a well-documented human carcinogen, a potentially effective remedy with high restorative property against arsenic-induced toxic effects still eludes us. In the present study, therapeutic efficacy of aqueous garlic extract (AGE) was analyzed in terms of reducing arsenic burden, as well as recovery in the altered biochemical variables particularly suggestive of oxidative stress, *in vitro* and *in vivo*. AGE (2mg/ml) co-administered with 10μM sodium arsenite ($NaAsO_2$) attenuated $NaAsO_2$ induced cytotoxicity, reduced intracellular reactive oxygen species (ROS) level and decreased mRNA expression of stress response genes in human malignant melanoma A375 cells. Moreover, AGE application in $NaAsO_2$-intoxicated Sprague-Dawley rats resulted in a marked inhibition of tissue lipid peroxide generation; enhanced level of total tissue sulfhydryl groups and glutathione; and also increased the activities of anti-oxidant enzymes, superoxide dismutase and catalase to near normal. An increase in blood ROS level and myeloperoxidase activity in arsenic-intoxicated rats was effectively prevented by AGE co-administration. AGE was also able to counter arsenic mediated incongruity in blood hematological variables and glucose level. The restorative property of AGE was attributed to its arsenic antioxidant activity, chelating efficacy, and/or oxidizing capability of trivalent arsenic to its less toxic pentavalent form. Taken together, evidence indicates that AGE can be a potential protective regimen for arsenic mediated toxicity.

Pathophysiology of Oral Submucous Fibrosis (OSF): Oral submucous fibrosis (OSF) is a precancerous condition of the oral cavity & oropharynx, a significant number of which transform into oral squamous cell carcinoma (OSCC). Presently, diagnosis of OSF is assumed mainly through qualitative histopathological evaluation, and at the level of diagnostic molecular biology, the genetic marker is still elusive. This study evaluates histopathological changes in the epithelium and subepithelial connective tissue of OSF through quantitative digital image analysis in respect to specific candidate features. The analysis revealed that there are subtle quantitative differences in the histological images of OSF compared to normal oral mucosa (NOM). The thickness of the epithelium and cell population in its different zones, radius of curvature of rete-ridges and connective tissue papillae decreased but length of rete-ridges and connective tissue papillae, fibrocity and the number of cellular components (predominantly inflammatory cells) in the subepithelial connective tissue increased in OSF. This study establishes a distinct quantitative difference between (NOM) and OSF in respect to their histological features. This study was done in collaboration with Dept. of Electronics, IIT-Kharagpur.

Dr. Kunal Ray and group

Molecular Genetic Studies on Human Diseases : A few genetic diseases that are common in India have been targeted which include eye disorders (primary open angle glaucoma, POAG & oculocutaneous albinism, OCA), neurological disorders (Wilson disease & Parkinson's disease), and bleeding disorder (Haemophilia). A brief overview of the studies is provided below. The intent of the study is to understand the molecular basis of these diseases.

Eye Disorders: The human eye is a complex organ, comprising a number of different tissue types that are derived from all three embryological layers. It is not surprising, therefore, that the eye is one of the commonest sites of genetic disease. The importance of this group of disorders is also reflected in the simple fact that genetic eye diseases, both monogenic (caused by single gene defect) and genetically complex (caused by interplay of a number of genes and the environment), comprise the commonest causes of blindness in children and adults. We are involved in molecular genetic studies on (a) glaucoma, which affects 67 million people worldwide and about 1.5 million people are blind due to glaucoma; and (b) Oculo-cutaneous albinism (OCA), a group of autosomal recessive disorders characterized by deficient synthesis of melanin pigment, associated with common developmental abnormalities of the eye. It is one of the major causes of childhood blindness in India.

CYP1B1 has been implicated in primary congenital glaucoma (PCG). Recent studies suggest role of *CYP1B1* in primary open-angle glaucoma (POAG) as a modifier locus. In this context we investigated further the potential role of *CYP1B1* in POAG patients. For this purpose two hundred unrelated Indian POAG patients and 100 unrelated ethnically matched controls were enrolled in this study. Six mutations were identified in 9 patients and none of the controls examined. A homozygous mutation of a conserved residue (R523T), detected in a familial JOAG patient (lacking MYOC or OPTN mutations), cosegregated with the disease locus in autosomal recessive mode of transmission. All the novel mutations (R523T, S515L and D530G) were detected in a region of CYP1B1 that did not harbor any of the 34 point mutations implicated in PCG. Our observation suggests that on rare occasions *CYP1B1* may be primarily responsible for juvenile onset POAG by possible monogenic association, and emphasizes the importance of screening for mutation in the gene of JOAG patients that are determined not to harbor mutation in already characterized candidate genes and loci for POAG (Acharya et al, *Molecular Vision*, 12: 399-404, 2006). These studies have been done in collaboration with Regional Institute of Ophthalmology, Medical College, Kolkata; and Dristi Pradip, Kolkata.

The studies on Oculo-cutaneous albinism (OCA), covering thirteen ethnic groups of India, some representing >20 million people, revealed that among 25 OCA families 12 were affected with OCA1, and that these cases were primarily due to founder mutations in TYR. We detected nine mutations and eight SNPs in TYR, of which six mutations (five point mutations & one gross deletion) were novel. In contrast to most reports describing compound heterozygotes, the presence of homozygotes in 10 out of the 12 pedigrees underscores the lack of intermixing between these ethnic groups in India. Haplotype analysis suggested a few founder chromosomes causing the disease in the majority of the patients. Direct detection of the mutations prevalent in specific ethnic groups could be used for carrier detection and genetic counseling (Chaki et al, *Annals of Human Genetics*, 70: 623-630, 2006).

Neurological Disorders: Among neurological disorders our group works on Wilson's disease (WD), Parkinson's disease (PD) and dystonia. The focus of the study is to identify the molecular basis of the disease among Indians. The studies are conducted in collaboration with Bangur Institute of Neurology for clinical areas of the study. While our group is focused primarily on Wilson disease, studies on PD and dystonia are done with the Prof. Jharna Ray (SN Pradhan Centre of Neurosciences, Calcutta University) who is the principle investigator for the studies on latter two diseases.

Wilson's disease is an inborn error of copper metabolism due to mutation in the copper-transporting gene *ATP7B* and characterized by excessive copper deposition predominantly in the liver and brain. The frequency of the disease is about 1 in 5000 to 1 in 30000 live births and based on this estimate the carrier frequency is approximately 1 in 90. Wilson disease (WD) produces typical lesions in the brain, which can aid in diagnosis and therapy. We reported a drug-resistant WD case with atypical cerebral lesions with marked involvement of white matter as visualized on MRI scans. The diagnosis was confirmed by identification of mutations in the ATP7B gene. The case demonstrates an uncommon pathology-related cerebral copper accumulation and emphasizes the importance of genetic screening in the diagnosis of WD (Aikath et al, *Neurology*, 67: 878-880,

2006). We also devised a simple and effective srategies for detection of allele dropout in PCR based diagnosis of Wilson's Disease (Gupta et al, *Clinical Chemistry*, 52: 1611-1612, 2006).

Parkinson's disease (PD), the second most common neurodegenerative disorder, affects at least 1% of the population over the age of 50. However, very little information is available regarding the molecular basis of PD among Indians. Since the largest number of mutations has been detected in the Parkin gene among all known PD loci, we aim to use Parkin as the candidate gene to assess its role in PD-related pathogenesis in Indian patients. A total of 138 PD patients and 100 controls were recruited for the study from eastern India. A total of 18 nucleotide variants including 6 novel changes were detected. These include five missense mutations (Gln34Arg, Arg42Cys, Arg42His, Tyr143Cys and Arg334Cys) detected in 8 patients in heterozygous condition and a homozygous deletion encompassing exons 3 and 4 in two sibs affected with PD. Clinical features of the Parkin mutants were compared. Among eastern Indian PD patients, mutation in Parkin was identified in 7.24% cases (Biswas et al, *Parkinsonism & Related Disorders*, 12: 420-426, 2006).

Dystonia is a common movement disorder. The purpose of this study is to examine the relative distribution of the primary dystonia subtypes and identify mutation (s) in the DYT1 gene in Indian patients. Primary dystonia patients and controls, lacking any symptoms of the disease, were recruited for the study from eastern India. We observed that, unlike other reports, pain and/or tremor was more common in our sporadic patients than in familial cases. Three reported and two novel changes were identified in this gene. The homozygous genotype (G,G) for a missense variant (c.646G > C; Asp216His) was significantly over-represented in the patients compared with controls ($P < 0.05$). However, the commonly reported 3 bp deletion (904-906delGAG) was not detected. Our results suggest that the DYT1 gene might have a limited role in causation of dystonia in the Indian population (Naiya et al, *Acta Neurologica Scandinavica*, 114: 210-215, 2006).

Bleeding disorder: Currently our lab is engaged in molecular genetic studies on Haemophilia. This X-linked disease is caused independently by defects in Factor VIII and Factor IX genes resulting in Haemophilia A and Haemophilia B, respectively. Usually females carry and males are affected with the disease. At present the most practical approach to contain haemophilia relates to strategies for carrier detection and prenatal diagnosis.

We aimed to test a set of in Factor IX gene linked RFLP markers (DdeI, XmnI, MnlI, TaqI & HhaI), used worldwide for carrier detection, to estimate its heterozygosity in different population groups of India, and identify additional single nucleotide polymorphisms (SNPs) if necessary. A total of 8 population groups encompassing different regions of India, consisting of 107 unrelated normal females without any history of hemophilia B in the family and 13 unrelated obligate carriers were recruited in the study. Regions of F9 gene were amplified by PCR from genomic DNA of the donors followed by restriction enzyme digestion and/or sequencing as appropriate. Combined informativeness for the markers varied between 52-86% among normal females belonging to different geographical locations of India. Haplotype analysis revealed that the most prevalent haplotype lacked the restriction sites for all five RFLP markers. Screening regions of F9 gene that harbor 10 SNPs reported in dbSNP yielded only two SNPs, which increased the overall informativeness in each population group and heterozygosity in the obligate carriers for the disease from 38% to 69%. Our data show that heterozygosity of commonly used RFLP markers is remarkably variable across different regions of India. Thus prudent selection of the markers based on specific population groups including usage of additional markers is recommended for efficient carrier detection (Mukherjee et al, *Disease Markers*, 22: 327-334, 2006). The study has been conducted in collaboration with Centre for Cellular and Molecular Biology (CSIR), Hyderabad and Indian Statistical Institute, Kolkata. Also, we have improved assay for genotyping haemophilia A carriers with intron 22 dinucleotide repeat marker towards our goal for better efficiency of carrier detection (Saha et al, *Haemophilia*, 12: 200-201, 2006).

Predictive medicine using repeat and single nucleotide polymorphisms (CMM 0016)

This ambitious program is aimed to identify the single nucleotide polymorphism in genes in different population groups of India. Sequence variation in human genes is largely confined to single-nucleotide polymorphisms (SNP) and is valuable in tests of association with complex disease, susceptibility to infectious diseases and pharmacogenetics traits. This network program has been undertaken by six CSIR laboratories. We at IICB have collected blood samples from eleven populations groups for the discovery panel and fourteen population groups for the validation panel. Genotyping has been completed in the genes that are related to the diseases under study covering about 1500 genomic DNA samples for the selected SNPs. The analysis of the data and communication of a manuscript from the Indian Genome Variation Consortium is underway. In addition the allele frequency and genotype data are for specific genes are currently being used from the perspective of studying the diseases of interest in Indian population.

Functional analysis of spindle assembly checkpoint in oral cancer

Dr. Susanta Roychoudhury and group

The Spindle Assembly Checkpoint is one of the surveillance mechanisms that protect cells from genomic instability and prevents mis-segregation of chromosomes until all the kinetochores are properly attached with bipolar spindles. The spindle assembly checkpoint is executed by the Bub-Mad pathway proteins which prevents ubiquitin (Ub) -mediated degradation of regulators of sister chromatid cohesion by Anaphase Promoting Complex (APC/C). This pathway involves the *Mad1, Mad2, Mad3, Bub1, Bub3, BubR1, CDC20* and *Mps1* gene products. Defects in the spindle assembly checkpoint are thought to be responsible for an increased rate of aneuploidization during tumorigenesis. Despite a plethora of information on the correlation between BUB-MAD gene expression levels and defects in the spindle checkpoint, very little is known about alteration of another important spindle checkpoint protein, Cdc20, in human cancer and its role in tumor aneuploidy. We observed overexpression of *CDC20* in several oral squamous cell carcinoma (OSCC) cell lines and primary head and neck tumors and provide evidence that such overexpression of *CDC20* is associated with premature anaphase promotion, resulting in mitotic abnormalities in OSCC cell lines. We also reconstituted the chromosomal instability phenotype in a chromosomally stable OSCC cell line by overexpressing *CDC20*. Thus, abnormalities in the cellular level of Cdc20 may deregulate the timing of anaphase promoting complex (APC/C) in promoting premature anaphase, which often results in aneuploidy in the tumor cells.

Correlation between microsatellite instability phenotype and misMathch repair gene defects in head and neck cancer: A subset of head and neck squamous cell carcinoma (HNSCC) exhibits microsatellite instability (MIN) phenotype. We correlated the alterations in *hMLH1* and *hMSH2* genes in primary HNSCC tumors and leukoplakia samples with MIN phenotype. One hundred twenty three paired HNSCC tumor normal tissues and twenty seven leukoplakia samples were examined for the hypermethylation of *hMLH1* and *hMSH2* promoters. Randomly selected 63 out of 123 tumors and all 27 leukplakia samples were genotyped with 8 microsatellite markers to determine MIN. Fifty percent HNSCC tumors and 63% percent leukoplakia samples harbored hypermethylation at either or both *hMLH1* and *hMSH2* promoters. Adjacent normal tissues of methylation positive tumors also suffered hypermethylation of these two promoters at a high frequency (25 %). A positive correlation between tobacco habit and promoter hypermethylation was observed.

There is a correlation between the level of MIN and the frequency of promoter hypermethylation in case of dysplastic leukoplakia samples but no such trend was observed for the HNSCC tumors. Interestingly, high frequency of MIN^+ patients (HNSCC tumors and lekoplakia) exhibited hypermethylation both at the affected and adjacent normal tissues ($P = 0.007$). Tobacco habituated patients having promoter hypermethylation both at the affected and adjacent normal tissues were mostly MIN^+ ($P = 0.047$). Thus it may be suggested that

individuals with tobacco habit are more susceptible to promoter hypermethylation of *hMLH1* and *hMSH2* and if that occurs in the normal squamous epithelium of the head and neck region, then those tissues are likely to develop into tumors involving MIN pathway.

Studies on genetic toxicology

Dr. Ashok K. Giri and group

Antimutagenic and anticlastogenic effects of black tea polyphenols in multiple test systems: Animutagenic and anticlastogenic effects of black tea polyphenols theaflavins (TF) and thearubigins (TR) and the different franctions of TR were evaluated in vitro and in vivo in multiple test ststems. The anticlastogenic effects were also evaluated in the human lymphocyte culture against two known carcinogenic compounds i.e. Aflatoxin B1 and Benzo(a)pyrene. The overall results indicate that these two black tea polyphenols have significant antimutagenic and anticlastogenic effects (Halder et al., 2006).

Assessment of health effects and genetic damage in the arsenic exposed individuals: A study was conducted to explore the effect of arsenic causing conjunctivitis, neuropathy and respiratory illness in individuals, with or without skin lesions, as a result of exposure through drinking water, contaminated with arsenic to similar extent. Cytogenetic damage were also carried out from the lymphocytes of arsenic exposed population. It has been observed that although individuals with skin lesions were more susceptible to arsenic-induced toxicity and genotoxicity and individuals without skin lesions were also sub clinically affected and are also susceptible to arsenic-induced toxicity and genotoxicity when compared to individuals not exposed to arsenic (Ghosh et al., 2006; 2007).

Toxicogenomics: genetic polymorphism in Indian population to industrial chemicals, and development of biomarkers

Drs. Ashok K. Giri, Kunal Ray, Susanta Roychoudhury, Keya Chaudhuri and their groups

Assessment genetic variants in the skin lesion and no skin lesions individuals exposed to arsenic :Since only less than 15-20% of arsenic exposed population showed arsenic induced skin lesions, so it is assumed that genetic variants might play an important role in arsenic toxicity and carcinogenicity. Potential of allelic variants of various genes of arsenic toxicity pathway (GSTT1, GSTM1, GSTP1) and others (p53, ERCC2 and PNP) have been examined for association with the phenotypic alteration. No difference in allelic variants in GSTT1 and GSTP1 was observed between these two groups. Incidence of GSTM1 null gene frequencies was significantly higher in the no skin lesion individuals indicating a protective role of GSTM1 null in arsenic toxicity (Ghosh et al., 2006). The results of p53 polymorphism showed that arsenic induced keratosis has a significant association with the R/R and S/S allele. So R/R and S/S genotype has higher risk for development of arsenic induced keratosis (De Chaudhuri et al., 2006). ERCC2 is a nucleotide repair pathway gene, whose protein product has a helicase activity and plays a key role in mending DNA damage, especially those induced by inorganic chemicals. ERCC2 codon 751 polymorphism (A→C; Lys→Gln) is implicated in several types of cancer. We wanted to find out any possible association of ERCC2 codon 751 polymorphism with arsenic specific premalignant Hyperkeratosis. AA genotype was significantly over represented in the arsenic induced Hyperkeratosis exhibiting group, indicating that it is strongly associated with the development of arsenic specific precancerous Hyperkeratosis.

Plant protease inhibitor as a potential bio-pesticide

Dr. Samir Dutta and group

Winged bean (*Psophocarpus tetragonolobus*) is a leguminous plant and is a very rich source of protease inhibitors. Earlier we have reported cloning and expression of two serine protease inhibitor genes from winged bean. WbTI-1B, representing a chymotrypsin/ trypsin inhibitor, inhibits both chymotrypsin and trypsin by forming a 1:1 complex with both the enzymes, but not simultaneously, whereas, WbTI-2 inhibits only trypsin at the same 1:1 ratio. The recombinant proteins were equally active as that of their counter wild types. Both the gene sequences were submitted with the GenBank.

This time, through site directed mutagenesis, WbTI-1B has been converted to specific inhibitors for either chymotrypsin or trypsin. Viz., the mutant designated as mtWbTI-1B, inhibited chymotrypsin at 1:1 ratio but did not inhibit trypsin even at ten times higher concentration, whereas the other mutant named as mcWbTI-1B, inhibited trypsin at 1:1 ratio, but did not inhibit chymotrypsin even at much higher concentration. Fig.1 & 2 represents time dependent induction of the recombinant inhibitor and presence of the inserts for the two mutants in pTrc-99A expression vector respectively. Fig. 3 represents a comparative view of the wild type WbTI-1B (seeds), recombinant WbTI-1B (rWbTI-1B) and its two mutants, mcWbTI-1B and mtWbti-1B after SDS-PAGE.

Since these inhibitors have proved to be detrimental against the polyphagous pest *Helicoverpa armigera*, integration and expression of these genes in plants affected by these pests have been conceived for initiation in the next phase.

Technical staff

Bhaskar Basu, Tapas Chaudhury, Rajat Banerjee (on E.O.L.)

Administrative staff

Mahua Bhattacharya

Pool Officers, RAs, Research Fellows

Dr. Susri Roychoudhury, Dr. M J Mukhopadhyay, Paromita Roychoudhury, Raghunath Chatterjee, Arunava Bandyopadhaya, Sumit Ranjan Das, Pratim Chaudhuri, Rajdeep Chowdhury, Ishita Chattopadhyay, Saibal Mukherjee, Moulinath Acharya, Ashima Bhattacharjee, Moumita Chaki, Arnab Gupta, Atreyee Saha, Suddhasil Mookherjee, Mainak Sengupta, and Poonam Nasipuri, Srikanta Goswami, Saibal Chatterjee, Sudarshana Basu, Bidesh Mahata, Pratik Home,Gunjan Dhar, Saikat Mukherjee, Biraj Mahato, Gourish Mondal, Meenakshi Chakravorty, Shiladitya Sengupta, Chaitali Mishra, Taraswi Banerjee, Deepanjana Dutta De, Swati Bajaj, Somsubhra Nath and Pinaki Mondal, Sanhita Roy, Nilanjana Bhattacharjee, Dipika Roy, Pritha Ghosh,Babli Halder, Sujata De Chaudhuri, Mayukh Banerjee, Nilanjana Banerjee, Udayan Bhattacharya

Drug Development, Diagnostics & Biotechnology

Drs. Tarun Kumar Dhar, Mina Mukherjee, Rajan Vedasiromoni, Anil Ghosh, Smita Mitra, Aparna Gomes, Nirmalendu Das, Pratap K. Das, Suman Khowala, Sharmila Chattopadhyay, Snehasikta Swarnakar

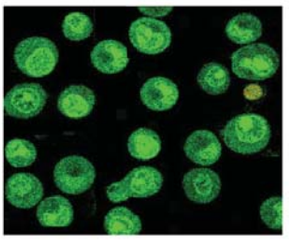
This group is involved in both basic and applied biological research covering various topics within the areas of health and process biotechnology. The main research focus is to promote development of new products, processes and technologies of commercial and industrial importance. The major field of activity includes - therapeutics principles from plants and venoms; mechanism of gastric ulceration; immunodiagnostic strategies; liposomal drug delivary; mushroom sporulation; trehalose metabolism; microbial glycosidase enzymes and engineering plant genes for improved production of pharmaceuticals/nutraceuticals.

Development of drugs from plant materials, animal products and synthetic agents

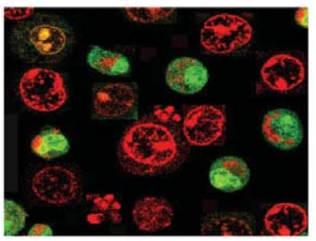
Dr. J. Rajan Vedasiromoni, Dr. (Mrs.) Smita Mitra Dr.(Mrs.) Aparna Gomes and group

Pharmacological studies with aqueous methanolic extract of *Swietenia mahagoni* leaves were carried out giving special emphasis to the anti-inflammatory and anti-cancer activities. The study revealed that the extract possesses potent analgesic and antipyretic activities and produced significant anti-inflammatory activity in acute, sub-chronic and chronic models of inflammation in rodents. It is plausible that the extract inhibited inflammation by blocking the cyclooxygenase pathway of arachidonic acid metabolism. A series of experiments had proved that the mahagoni leaf extract inhibited the growth and metabolic activity of human leukemic cell lines U937, K562 and HL-60 in a concentration and time-dependent manner and also induced apoptosis as has been confirmed by fluorescence and confocal microscopic studies.

The anti-inflammatory activity of *Litchi chinensis* leaves has already been reported. The aqueous methanolic extract of *Litchi chinensis* leaves was evaluated experimentally for its *in vitro* anti-cancer activity. It was found that the extract inhibited cell growth and metabolic activity of U937, K562 and HL-60 cell lines in a concentration- and time-dependent manner. Fluorescence microscopic studies of the cells showed that the litchi leaf extract induces apoptotic changes which was confirmed by confocal microscopic studies in which chromatin condensation, nuclear fragmentation and formation of apoptotic bodies were observed (Figs. 1 & 2).

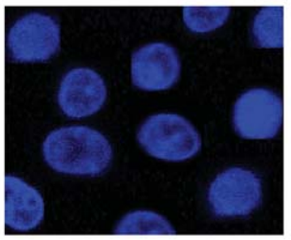


1A

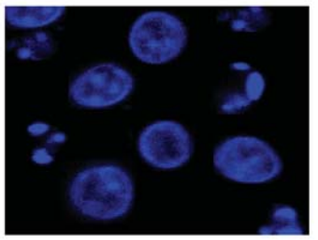


1B

Fig. 1. Fluorescence microscopic study of HL-60 cells. 1A -control cells, 1B- *Lichi chinensis* leaf extract treated cells showing apoptotic changes.



2A



2B

Fig. 2. Confocal microscopic study of U937 cells. 2A- control cells, 2B- *Lichi chinensis* leaf extract treated cells showing formation of apoptotic bodies.

The methanolic seeds extract of *Swietenia mahagoni* Jacq. was also investigated experimentally for anti-inflammatory, analgesic and antipyretic activities and it was found to possess potent anti-inflammatory, analgesic and antipyretic activities. The study revealed that the anti-inflammatory activity is mediated through inhibition of cyclooxygenase pathway of arachidonic acid metabolism.

Involvement of reactive oxygen species (ROS) as a causative factor in human gastric carcinogenesis was studied. Inflammation causes accumulation of activated neutrophil, which produces excessive ROS through oxidative burst. Thus the extent of neutrophil involvement as indicated by its myeloperoxidase activity was measured (Table 1). Indirect evidence of involvement of ROS in gastric carcinogenesis was clarified by measurement of lipid peroxidation and protein carbonyl content indicative of oxidative damage of lipid and protein respectively (Table 2). Since chronic atrophic gastritis is believed to be a precursor of gastric cancer, to identify whether ROS has any role in progression of the disease; the oxidative damage of gastritis tissue was also studied. Lipid peroxidation and protein carbonyl content increases progressively from control to gastritis to gastric cancer. However neutrophil accumulation was similar in both the cases.

Table 1. Myeloperoxidase activity was measured by TNB assay using Cl^- as electron donor

Myeloperoxidase activity in human gastric mucosa in relation to H.pylori infection				
TNB oxidized (nmoles/min/mg protein)				
	H. pylori negative	n	*H. pylori positive*	n
Control	22(5.3	17	81(17	7
Gastritis	65(16#	5	126.5(13**	6
Gastric cancer	66(16#	17	114(24**	9

#p<0.02 vs control; ** p<0.05 vs control

Table 2. Lipid peroxidation of the gastric mucosal homogenate was measured as the thiobarbituric acid reactive substances (TBARS)

Oxidative damage of human gastric mucosa				
	TBARS (nmoles/mg)	n	Protein carbonyl contenta (nmoles/mg)	n
Control	0.7 (0.04	14	0.04 (0.003	14
Gastritis	1.01 (0.04*	19	2.68 (0.67*	12
Gastric cancer	4.02 (0.75*	14	7.87 (1.73*	12

[a]Protein carbonyl content was measured according to Levine et al. *p<0.001 vs control

In the previous year, the *in vitro* anti-cancer activities of TRE and two of its triterpenoid saponins, TS1 & TS2, were well established. In vivo anti-cancer studies carried out revealed the anti-tumor effect of TRE against Ehrlich ascites carcinoma in Balb-C mice. A significant dose-dependent enhancement of the mean survival time (MST) was observed. The anti-tumor effect of TRE was more pronounced than 5-fluorouracil (5-FU), the reference anti-tumor agent. The investigation has shown that TRE possess an *in vivo* apoptogenic effect. Morphological investigations including transmission electron microscopy proved that TRE caused nuclear granulation, which is the indication of apoptosis. Furthermore, flow cytometry and dot plot analysis confirmed the induction of apoptosis by TRE in EAC cells with comparatively less effect on cell cycle (Fig. 3). Moreover, TRE was found to possess antioxidant efficacy increasing serum alkaline phosphatase and SOD in EAC mice but the extract was found to possess no effect on glutathione related enzymes in mice.

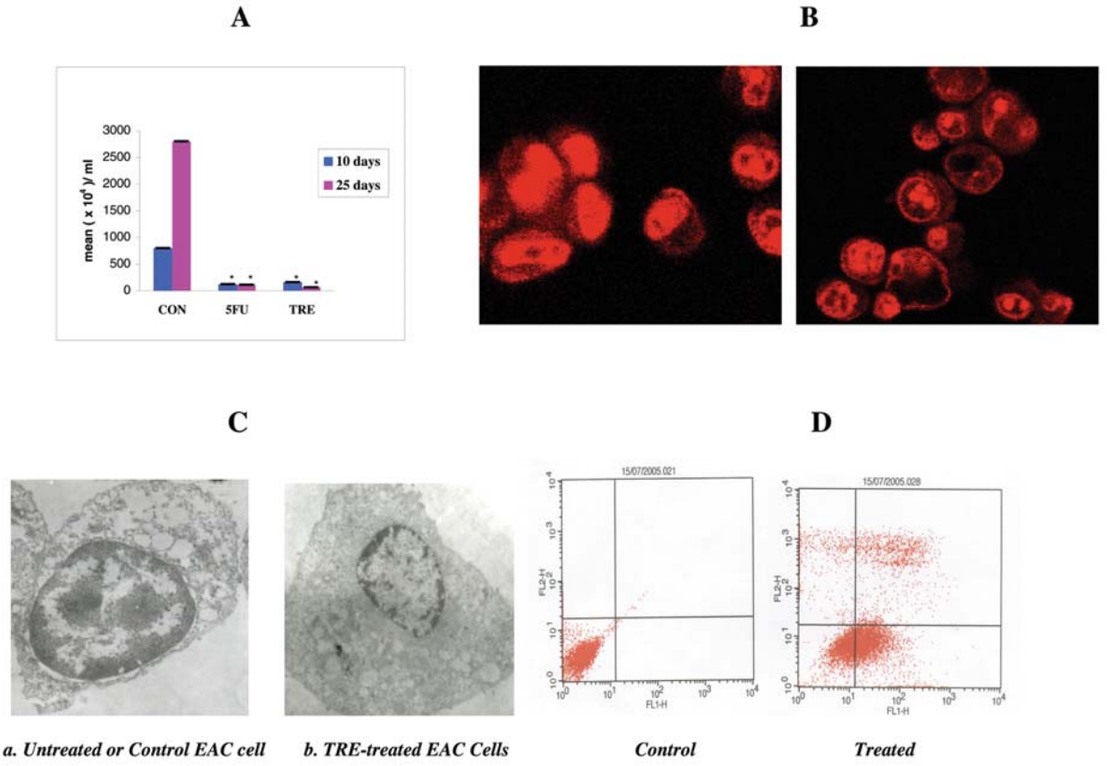


Fig. 3. Effect of TRE on EAC cells. (A) Effect of TRE on cell count of EAC in mice peritonium after 10 & 25 days treatment, (B) Confocal Microscopic photographs of EAC cells stained with propidium iodide, (C) TEM of EAC cells (original magnification, 25000X), (D) Flow-cytometry & dot Plot assay after 24 hrs. *in vitro* treatment with TRE with EAC, % of apoptotic cells are given: Con (0.16%), TRE (38.12%)

A cytotoxin NK-31 has been purified from the Indian monocled cobra (*Naja kaouthia*) venom by CM cellulose Ion Exchange Chromatography. Homogeneity of NK-31 was confirmed by RP-HPLC and the SDS-molecular weight was found to be 6760 D. The N-terminal amino acid sequence (first 20) was KCNKLVPLFYKTCPAGKNL. It significantly inhibited proliferation of U937/K562 cells. IC50 value on U937/K562 cells was 3.5µg/ml and 1.1(g/ml respectively. Scanning and confocal microscopic studies showed typical features of apoptosis (disrupted plasma membrane and nuclear condensation) in treated cells. NK-31 treatment produced significant early/late apoptosis of U937/K562 cells observed through FACS analysis and produced significant cell cycle arrest at sub G1 phase (Fig. 4.) The compound is a strong cardiotoxin as it (30 µg/ml) causes blockade of isolated guinea-pig auricle in 4±1.15 min (Fig. 5). NK-31 induced guinea pig auricular contraction blockade time was significantly reduced at low Ca^{2+}, high Na^{+} and EDTA concentration.

Mg^{2+} and K^{+} produced no effect on NK-31 induced cardiotoxicity. However, in presence of trypsin, NK-31 lost its cardiotoxicity. It did not produce blockade of stimulated rat phrenic nerve diaphragm. NK-31 (low dose i.e. 1/8th LD50 and medium dose i.e., 1/4th LD50) did not produce sub-chronic toxicity when used to treat (i.p) normal adult Balb-C albino mice for 28 days. Haematological and biochemical parameters were maintained within normal limits. The compound did not have any haemolytic activity when examined on mice, guinea pig, goat and human erythrocytes. The study brings into light that the anticarcinogenic component identified from the Indian cobra venom was a low molecular weight cardiotoxin but showed no long-term toxic effect at sub lethal concentrations. Further detailing of the study may unveil more interesting facts regarding this toxin from the venom of an Indian snake species and pave the pathway towards novel drug development.

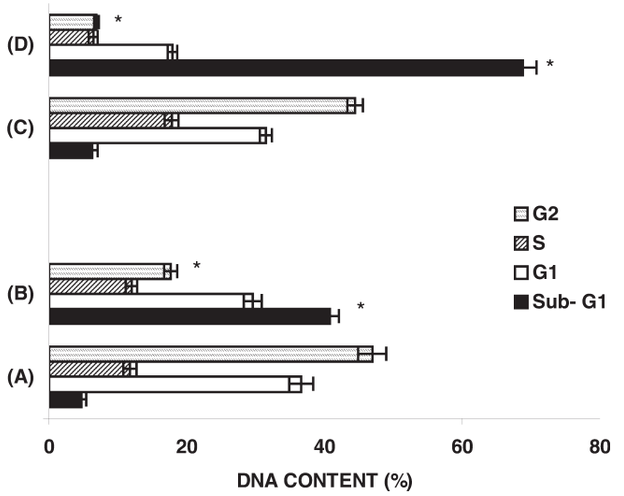


Fig. 4. Effect of NK-31 (IC50, 24 hrs) on cell cycle of U937 and K562 cells. Values are mean of percentage DNA in each phase of cycle (SE (n=4). (A, B)- U937 Control & treated; (C, D)- K562 Control & treated. *Significant change as compared to control ($p<0.05$). Data represents a sub-G1 arrest of the leukemic cells after NK-31 treatment within 24 hrs.

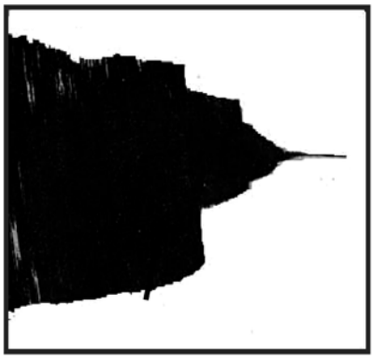
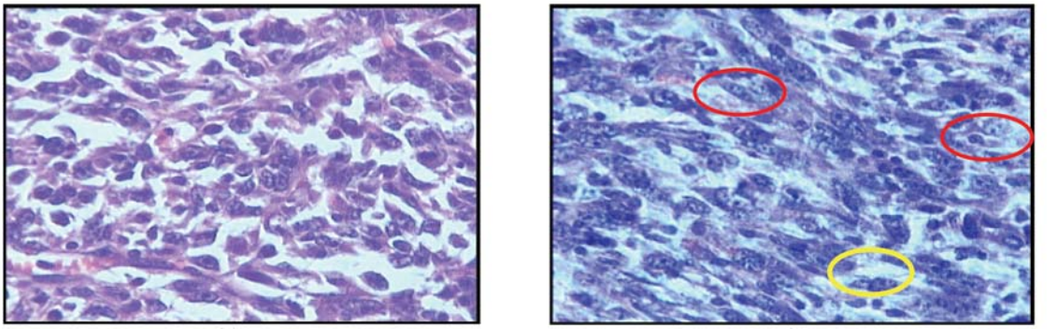


Fig. 5. Effect of NK-31 on isolated gunieapig auricle. Auricular contraction was blocked within 2 min of NK-31 injection.

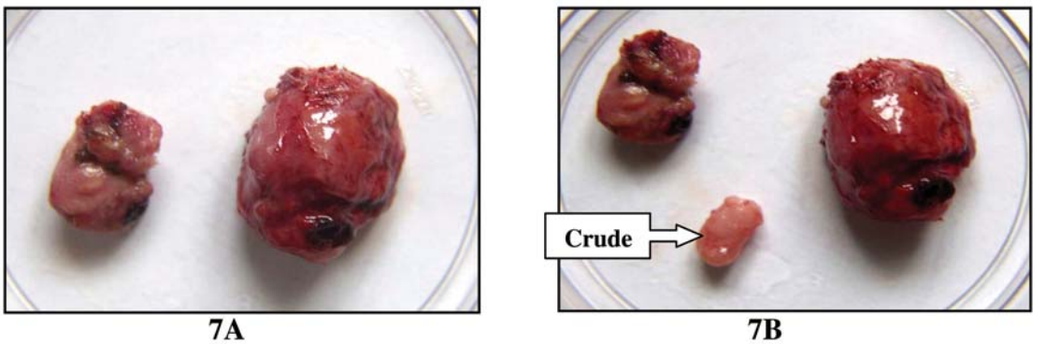
Indian black scorpion (*Heterometrus bengalensis*) venom was used to assess its cytotoxic and anticancer properties. Crude venom was dissolved in physiological saline and used against murine solid tumor and Ehrlich ascites carcinoma model. Venom treatment significantly reduced the intraperitoneal EAC cell count by 57.26%. After completion of venom treatment, blood and liver from the mice were obtained to measure various biochemical parameters. Serum alkaline phosphatase level was increased but serum glutathione level was not affected. Liver glutathione transferase level was increased in venom treated group, but venom action significantly reduced lipid peroxidase activity. However, the liver gluathione peroxidase level remained unchanged in the envenomed animals.

The venom significantly reduced tumor weight and volume in solid tumor model. There was a significant change in histopathological observation in treated animal when compared with control. The results obtained suggest that the venom has antiproliferative effect on solid tumour growth by reducing tumor weight and volume. It also reduced tissue damage as shown by histopathological observations (Figs. 6, 7 and 8). Heterometrus bengalensis venom showed positive action on 20-methylcholanthrene induced solid tumour in mice. Work is under progress to isolate the active compound responsible for such antiproliferative activity.



6A 6B

Fig. 6. Histolopsthology of solid tumor: 6A represents section from the control tumor showing prominent angiogenesis, **6B** represents tumor section from crude venom treated mice showing distinct karyolysis (red circles) and vacuolizations (yellow circle).



7A 7B

Fig. 7. Effect of crude venom on tumor size: 7A represents tumors from two control mice; **7B** shows the tumor dissected out from the crude venom treated animal as compared to the control counterparts.

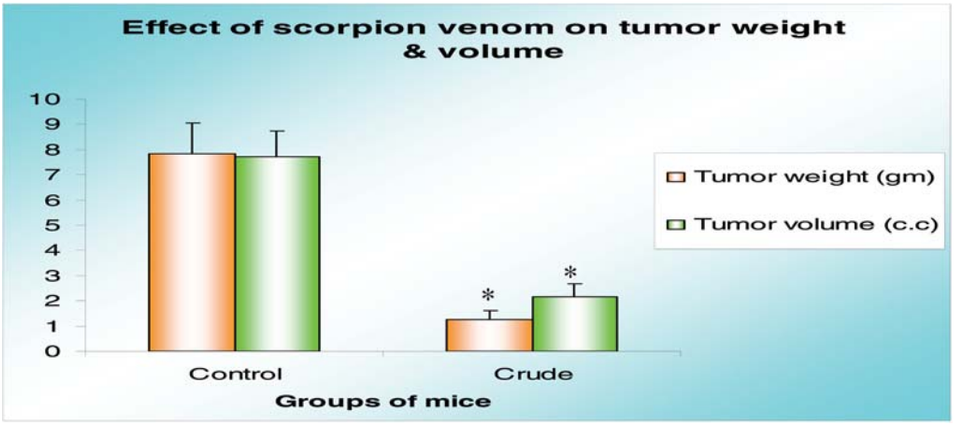


Fig. 8. Data representing the significant decrease in tumor weight and volume by crude *Heterometrus bengalensis* venom treatment.

Screening of Indian biodiversity and Indian Systems of medicine for anti gastric ulcer principle(s)

Dr. Pratap K. Das and group

In continuation of the development of appropriate strategy and protocol(s) for effective screening of Indian biodiversity including Indian medicinal plants, bacterial and fungal extracts, marine resources, and Indian Systems of Medicines like *Ayurvedic & Siddha* preparations, and also synthetic as well as naturally isolated single molecules for their efficacy against peptic ulcer diseases, we have recently added gastric parietal cell based assay for antisecretory activity evaluation and in vivo chronic *H. pylori* infection model in our repertoire of evaluation models. The central objective of this programme has been to dovetail traditional knowledge base and information systems with the help of currently understood biological targets to generate newer leads, and transfer such know-how to national and multinational pharmaceutical companies for commercial exploitation.

During the period under consideration, we have screened about 2200 samples from plant, bacterial and fungal origin as well as a few traditional preparations and single molecules in gastric antisecretory and anti *H. pylori* models. We could primarily fish out about five plant samples, two microbial extracts, one *Ayurvedic* and two *Siddha* preparations as well as nine single molecules as active. We are reexamining them with repeat collection and repeat extraction to validate the primary findings, and to take the sample(s) to next stage of investigation through bioassay-guided fractionation approach. Meanwhile, previously screened samples that have been revalidated during the period under consideration yielded two plant extracts as lead antisecretory agents, and one single molecule as lead anti *H. pylori* agents for further development through drug discovery exercises.

One such lead extract (ICB-A002) and a single molecule CPP-1 were examined in chronic in vivo *H. pylor*i infection model, which indicated potential for the extract when used in combination with antibiotics to clear and eradicate *H. pylori* burden (Fig. 9). The extract is now being developed for IND filing and commercialization. The molecule CPP-1 (a semi-synthetic flavone), on the other hand, is showing promise to be a bifunctional agent killing *H. pylori in vitro* as well as blocking gastric HCl secretion in parietal cell based assay. The extensive morphological degeneration of the bacteria in presence of MIC-MBC dose was evident in fluorescence and electron microscopic study (Fig. 10).

We are in the process of developing the screening model for evaluation of various primary leads in gastric cancer cell lines, essentially following the NCI guidelines, taking cell viability as the measuring parameter employing trypan blue exclusion and MTT assay. Determination of mutagenicity profile of the active samples is in the process.

Under Drugs & Pharmaceuticals Programme of DST, a research programme is under progress with Funds from DST and an Industry, M/s Dey's Medical. In this inter-institutional programme entitled *'Chemical Standardization & Biological Evaluation with a View to Increase Efficacy of Herbal Medicines'* wherein 3 products of the company are

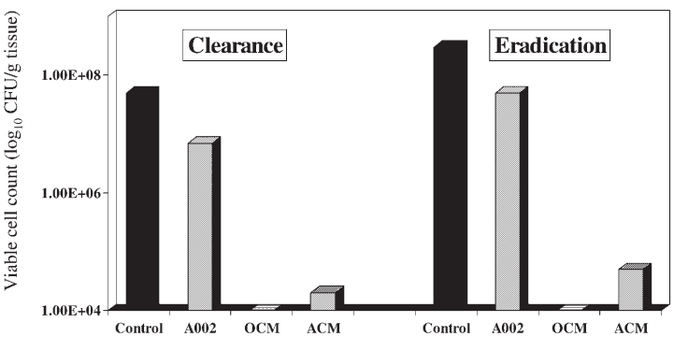


Fig. 9. Effect of ICB-A002 on *H. pylori* induced chronic infection model in C57BL/6J mice. Each mouse was inoculated with 0.1 ml SS1 strain (108 cfu) three times over five days. Two weeks following infection, A002 monotherapy (1g/kg/day), or standard triple therapy OCM (OCM: 400 (mole/kg/day omeprazole, clarithromycin: 7 mg/kg/day and metronidazole: 14 mg/kg/day) or designed triple therapy ACM (A002: 1 g/kg/day, clarithromycin: 7 mg/kg/day and metronidazole: 14 mg/kg/day) were given twice daily for 7 days. Half of the animals were sacrificed after 36 h and the rest after 29 days of the last treatment. Clearance indicates reduction in bacterial load 36 h after the cessation of treatment, whereas eradication indicates the same 29 days after the treatment, both being measured in terms of log10cfu/g.

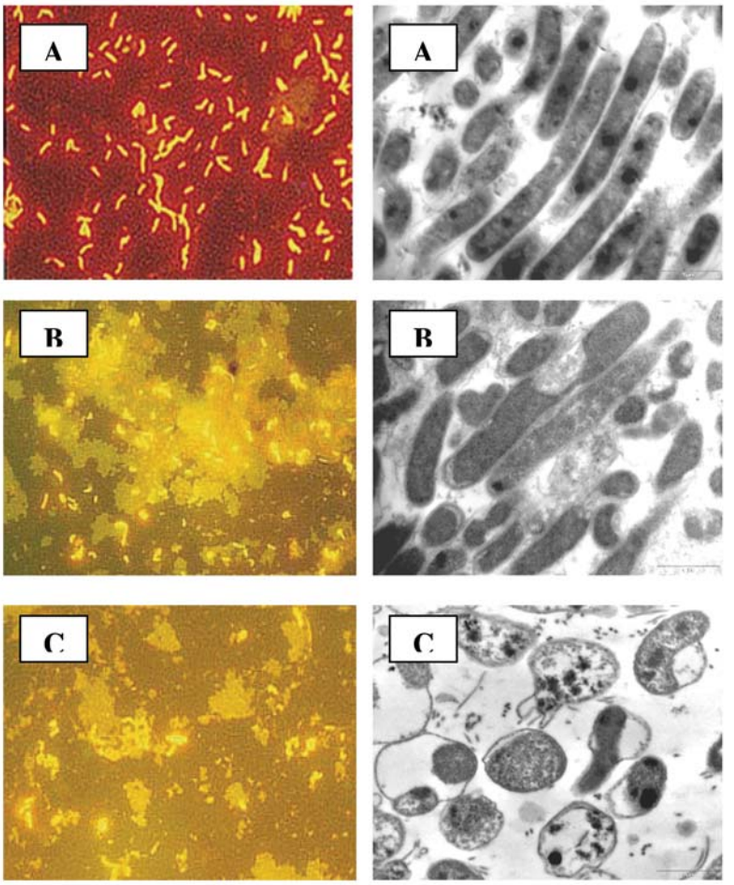


Fig. 10. Morphological transformation of *H. pylori* upon 24-h exposure to increasing concentrations of CPP-1. Two strains, a clinical 80A strain and a standard ATCC 43504 strain were incubated in biphasic culture condition under microaerophilic environment in the presence and the absence of CPP-1 (A-1 & A-2 control, B-1 & B-2 6.25 (g/ml and C-1 & C-2 12.5 (g/ml). After 24 h, 10 ml cell suspension was processed for microscopic evaluation. Left panel represents fluorescence microscopic picture (1000X) with strain 80A and the right panel shows the transmission electro microscopic picture (16,500X) with ATCC 43504.

being scientifically examined for their efficacy. 'Trasina' is one such anti-stress anti-aging product of the company, which was examined in vivo for cold-restraint stress-induced gastric ulceration. The product was found to be effective in ameliorating such stress ulcer. The purpose of such R&D tie up of DST-Industry-IICB has been to find out the modern scientific basis of these traditional medicines that would permit them to compete in national and international market under the changed global scenario of Drugs and Pharmaceuticals sector in the era of patent, and IPR.

The overall impact of such programme will have its bearing on the development of better, safer and cheaper anti-ulcer medicines from alternate sources. Future studies will be initiated towards development of a few more new-biology based models, like gastric cancer cell culture, so as to be able to be globally competitive in such drug development programme of revisiting Indian biodiversity.

Role of matrix metalloproteinases in remodeling of extracelular matrix of gastric tissues during inflammation: Mechanism of action of antioxidants

Dr. Snehasikta Swarnakar and group

Our long term goal is to investigate the molecular mechanism of gastric ulcer for understanding the therapeutic potential of bioactive molecules for blocking gastric ulcer. Our focus is to elucidate the role of matrix metalloproteinases (MMPs) during gastric ulceration and healing. MMPs, a family of zinc dependent endopeptidases attribute greatly to the extensive changes in the extracellular matrix (ECM) that occur during several diseased conditions. However, the regulation of MMPs during gastric ulceration and the mechanistic basis is still unclear. Curcumin (a bioactive constituent of turmeric), melatonin and famotidine have been found to have significant anti-ulcer activity through MMP-dependent pathway in non-steroidal anti-inflammatory drug-induced and ethanol-induced gastric ulcers. Our studies also emphasize on the role of MMPs in H. pylori-infected as well as diabetic gastric ulcer and mode of action of antioxidants during healing of diabetic gastric ulcer as well as wound. The other project in our laboratory focuses on regulation of MMPs expression by oxidative stress in endometriosis, a gynecological disease of women. An increased activity and expression of MMP-9 and -3 along with decreased expression of tissue inhibitors of metalloproteinases-1 has been observed with the severity of endometriosis.

Over the past few years our understanding of gastric ulcer has largely been outlined in studies on extracellular matrix (ECM) remodeling. Melatonin's action is examined on ECM remodeling during prevention of NSAID-induced gastric ulcer (J. Pineal Res. 43, 56-64, 2007). We document MMP-9 upregulation in ethanol-induced gastric injury and famotidine, a H2-receptor antagonist, arrests MMP-9 elevation (Fig. 11).

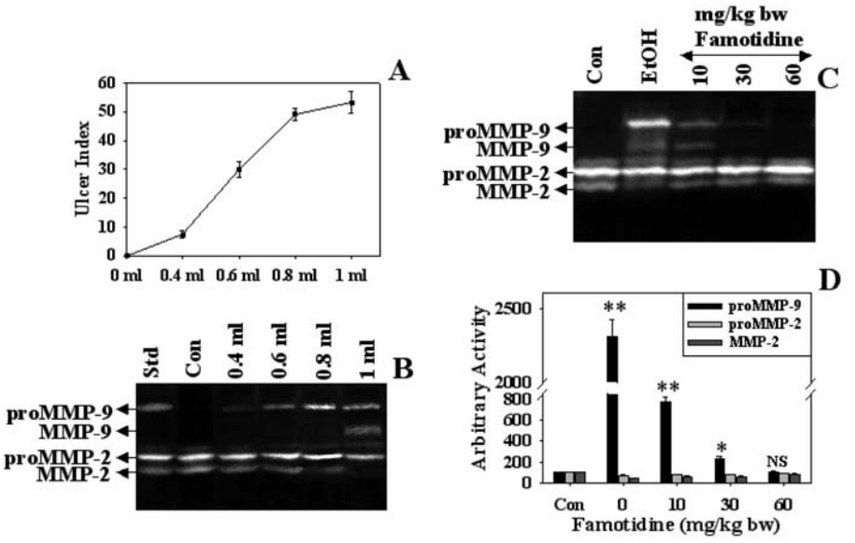


Fig 11. Effect of ethanol on MMP-9 and -2 activities in rat gastric tissues and effect of famotidine thereon. Varying doses of 70% ethanol were administered orally to different groups of rats, sacrificed after 3 hours and ulcer index were scored. Control group received only sterile water. (A) Mean ulcer index from each group of rats was plotted against

respective doses of ethanol. (B) Gelatin zymography was performed using equal amounts (80µg protein) of PBS extracts of ulcerated tissues to detect MMP-9 and -2 activities. Different doses of famotidine were fed orally to separate groups of rat prior to 0.8 ml, 70% ethanol treatment and sacrificed after 3 hours. (C) Gelatin zymography of PBS extracts of gastric tissues from famotidine pretreated-ethanol treated group of rats. (D) Histographic representation of famotidine doses against arbitrary activity values of proMMP-9 and MMP-2 as measured by Lab Image software from the above zymogram and two other representative zymograms from independent experiments. Error bars = (SEM. (, p(0.001, control vs. ethanol and ethanol vs. famotidine.

It indicates an alternative biochemical mechanism of famotidine for implication in gastroprotection. We examined mouse gastric tissues for expression of MMPs following infection by cag+ve and cag-ve strains of *H. pylori* (J. Biol. Chem. 281, 34651-62, 2006). Mice either infected with cag+ or cag- *H. pylori* strains showed gastric inflammation (Fig. 12) and significant upregulation of proMMP-3 expression in gastric tissues (Fig. 13). We tested human endoscopic samples for MMP-9 expression and found that MMP-9 is significantly high in *H. pylori* infected ulcerated tissues compared to that of non-ulcerated tissues (Fig.13). Mechanism of action of antioxidants (e.g. curcumin, melatonin, N-acetyl cystein and *Azadiracta indica* leaf extract) in preventing gastric ulcers is another major interest of research. Attempts to understand the regulation of ECM remodeling by antioxidants in ulcer healing will lead to better understanding of molecular mechanism of the disease and open up avenues to arrest the disease without recurrence.

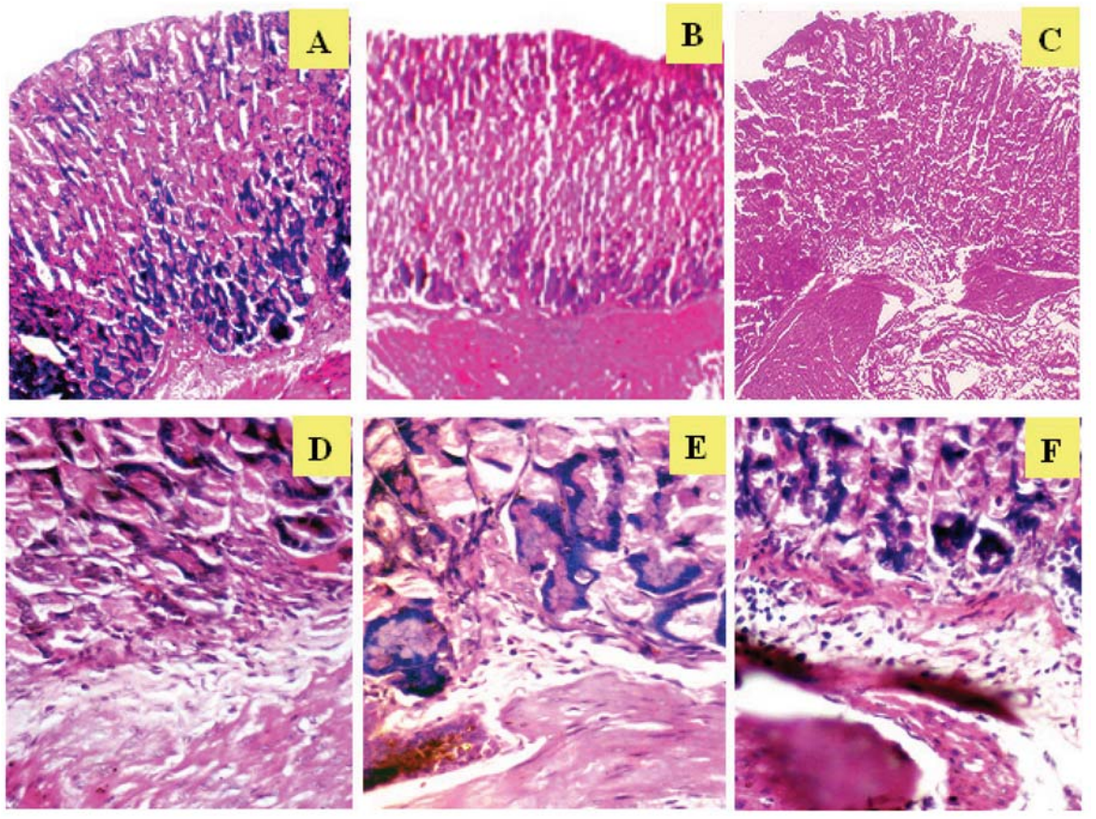


Fig. 12. Mouse gastric tissues following infection with cag+ve and cag-ve *H. pylori* strain. Different groups of mice were orally infected with SS1 (cag+) and AM1 (cag-) strains of H. pylori, sacrificed on day-10 post infection and stomachs were sectioned for histological studies. Control mice were fed with PBS and kept separately under the same conditions. Histological appearances of control (A), AM1 infected (B) and SS1 infected (C) gastric tissues stained with hematoxylin and eosin and were observed at 20 X 10 magnification. While (D), (E), (F) represent control, AM1 and SS1 infected tissues at 40 X 10 magnification.

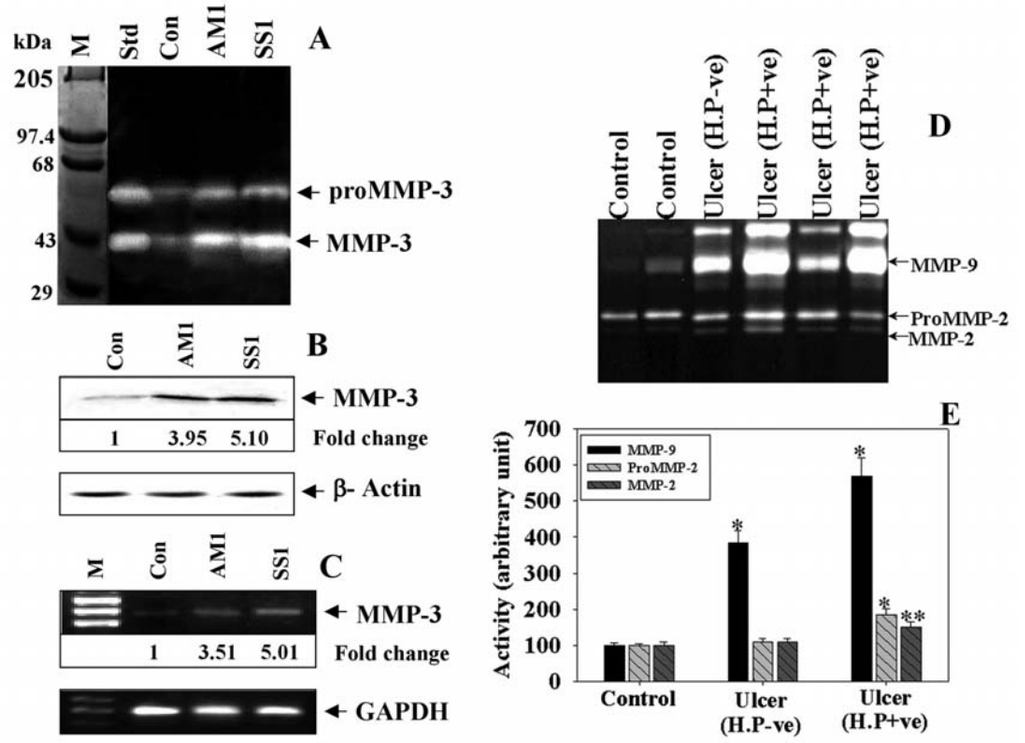


Fig. 13. Upregulation of MMP-3 and MMP-9 activity in *H. pylori* infected AGS cells in culture and human biopsy samples respectively. Different strains of H. pylori (SS1 and AM1) were orally fed separately to two groups of mice while control mice were fed with PBS and they were sacrificed on day-10 post infection. (A) Casein zymography of PBS extracts of control and infected mouse gastric tissues. (B) Western blots of PBS (100 (g protein) extracts from control and infected tissues and probed with polyclonal anti-MMP-3 antibody and monoclonal anti-β-actin antibody. (C) RT-PCR analysis of MMP-3 mRNA expression in control and infected mice. PCR using GAPDH primers was done as positive control. Human biopsy samples from control and ulcerated with H. pylori negative and positive were collected and subjected to tissue extraction. (D) Gelatin zymography was conducted using equal amounts (25µg) of PBS extact of human biopsy samples (E) Histographic representation of MMP-9 and proMMP-2, MMP-2 activities as quantified using Lab Image software designed densitometry from the Fig D zymogram and two other representative zymograms from independent experiments. Error bars = (SEM. *p < 0.01 and **p < 0.001 versus control, NS, p=not significant vs. control.

Development of ultrasensitive enzyme immunoassay

Dr. T. K. Dhar and group

Enzyme immunoassay is now a widely used technique for the detection and quantification of different substances. The sensitivity of this technique has not, however, always been completely satisfactory and long incubation periods are often required to generate significant signal intensities for accurate estimation of analytes. The catalyzed reporter deposition (CARD) method of signal amplification, also called "tyramide signal amplification", has been used in immunoassays not only to increase sensitivity but also to reduce assay time. The method is based on the ability of horseradish peroxidase (HRP) molecules to oxidize the phenol moiety of the added biotinylated tyramide (B-T), which react covalently with electron-rich moieties of protein molecules present in the vicinity of the HRP label. Few years ago, we reported an improved CARD method of signal amplification termed 'Super-CARD', which was similar to CARD except it uses synthesized electron-rich protein instead of casein to block vacant sites of the membrane. The method markedly increases the HRP-catalyzed deposition

of B-T, which amplifies the signal and increases the assay sensitivity. The main disadvantages of these amplification methods are liquid-phase treatment of reagents based on slow incubation with agitation and several manipulations of the membranes.

We have developed a new filtration-based tyramide amplification and substrate visualization techniques using aflatoxin B1 (AFB1) as a test analyte. The method has been tested with an improved membrane test device and involves sequential filtration of standards or sample, AFB1-HRP conjugate, B-T, avidin-HRP, and substrate solution over anti-AFB1 antibody-spotted zones of the membrane surface (Fig. 14).

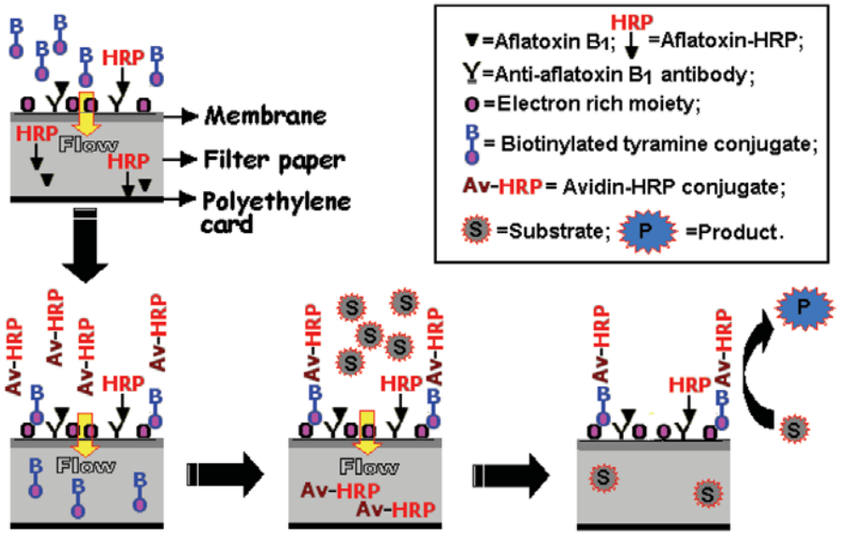


Fig. 14. The principle of filtration-based tyramide signal amplification technique.

We investigated the effect of filtration of B-T and substrate by AFB1 assay. The results showed dramatic increase in spot intensity at each B-T concentration compared with that achieved by use of the standard pouring-agitation procedure (Fig. 15). The calculated percentage difference between filtration and pouring-incubation method for each B-T concentration for CARD and Super-CARD methods revealed enhancement of spot intensity (740 and 370% over standard CARD and Super-CARD methods, respectively), which was maximum at the lowest B-T concentration (12.5 µmol L-1). To determine the individual amplified response of the substrate, B-T was added by the pouring-incubation method and the substrate by filtration. The results showed acceleration of spot intensity was maximal at the lowest B-T concentration and decreased only gradually with increasing B-T concentration. Thus, this filtration-based approach of B-T or substrate addition markedly improved spot intensity even though the amounts of reagents used were reduced by a factor of 50 compared with the standard method.

The techniques have been used for rapid detection of AFB1 in a variety of foodstuffs with a detection limit of 12.5 µg/kg. The method based on filtration technique saves time, improves reproducibility, eliminates many washing steps and avoids manipulation of the membranes between the different steps, while maintaining the sensitivity of the pouring-incubation method. Average recoveries from different non-infected food samples spiked with AFB1 at concentrations from 25 to 100mg/kg were between 95 and 105%. AFB1 results obtained on different days for Aspergillus parasiticus infection of corn and groundnut samples correlated well with estimates obtained by HPLC.

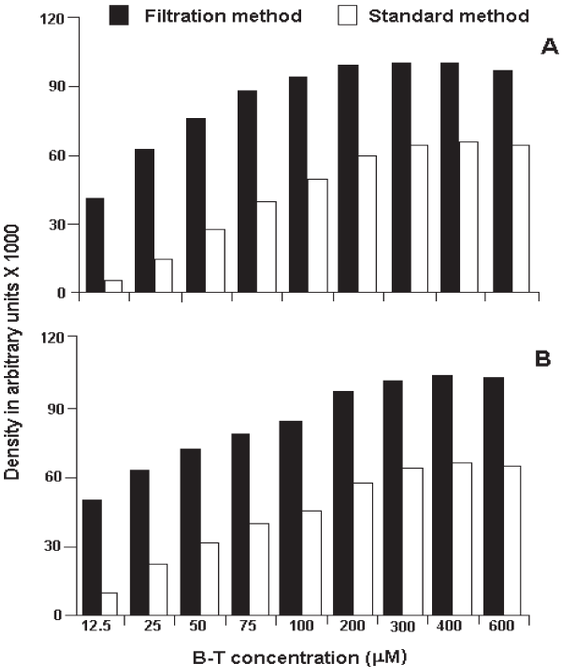


Fig. 15. Comparison of spot intensity obtained by densitometric analysis of buffer zero by AFB1 assay with different concentrations of B-T using CARD (A) and Super-CARD (B) amplification methods.

Liposomal flavonoid against cellular diseases

Dr. Nirmalendu Das and group

Formulation of mannosylated liposome intercalated polyphenolic herbal components was done to ascertain whether treatment with that formulation exert any neuroprotective effect against cerebral diseases. It has been demonstrated that mannosylated liposome encapsulated QC not only prevented cerebral ischemia and reperfusion induced lipid peroxidation and cerebral edema development but also protected cerebral endogenous antioxidant defence in young and old rat brain. This approach of delivering a non-toxic herb origin antioxidant (quercetin) to the brain offers the potential clinical application in human neurodegenerative diseases in future.

Studies were carried out to ascertain whether treatment with herb origin polyphenolic compound intercalated in galactosylated liposomes exerts any hepatoprotective effect against arsenic induced fibrosis in liver. The protective role of Quercetin (herbal polyphelnolic compound) in galactosylated liposomes against arsenic induced hepatotoxicity has also been confirmed. This approach of delivering a non-toxic herb origin polyphenolic compound QC selectively to the liver might be useful in therapeutic application to prevent arsenic induced liver fibrogenesis.

Further studies are planned to perform sub-chronic and chronic studies, in order to substantiate our claims that QC might be useful in therapeutic application in combating NaAsO2 induced fibrogenesis resultant from chronic arsenic exposure.

Biochemical Understanding of sporulation for the development of sporeless strains of oyster mushroom (Pleurotus spp).

Dr. Mina Mukherjee and group

The objective of the present is to understand the regulation of basidiospore formation in oyster mushroom, as the spores are known to be allergic to the cultivators. The knowledge might help to develop sporeless strains of oyster mushrooms.

The specific laccase substrate of Lacsp, produced at the time of sporulation in the gill tissues of *P. ostreatus* has been purified and characterized.

Purification and characterization of cellobiose dehydrogenase from culture filtrate of Termitomyces clypeatus. Cellobiose dehydrogenase is an industrially important enzyme. However, their application is restriced due to non-availability of the enzyme. The objective of the investigation is to search a new source of Cellobiose dehydrogenase. The optimum conditions for the production of the enzyme have been standardized. The cellobiose dehydrogenase (CDHtc) enzyme has been purified from the culture filtrate of *T. clypeatus* and partially characterized. The enzyme was found to be a hemoflavoenzyme (Fig. 16).

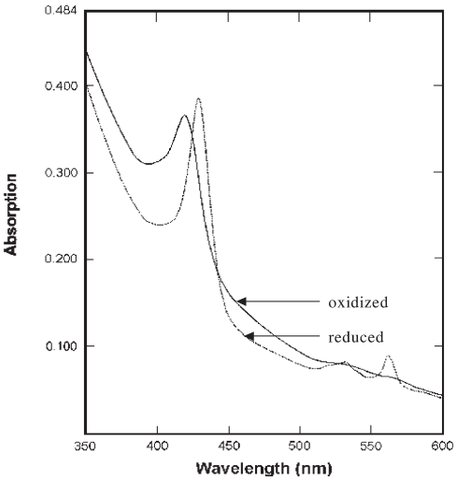


Fig. 16. Absorption spectrum of purified cellobiose dehydrogenase from *Termitomyces clypeatus* in the oxidized and reduced state. The reduction was performed with cellobiose.

Purification and characterization of trehalose-6-phosphate synthase from Saccharomyces cerevisiae

Dr. Anil. K. Ghosh and group

The enzyme complex - trehalose synthase, present in *S. cerevisiae*, was purified to homogeneity. N- terminal amino acid sequence of trehalose-6-phosphate (tre-6-p) synthase indicated 60% homology to reported amino acid sequence of *S. cerevisiae*. Physiochemical properties of the purified enzyme were studied and it was found 3-4 times activated by the presence of $ZnSO_4$. Studies on protein association- dissociation and folding are currently underway.

Purification of neutral trehalase from Candida utilis. There are two types of trehalase found in *S. cerevisiae*, viz. acid trehalase and neutral trehalase. Acid trehalase was reported to be necessary for extracellular trehalose utilization. We have previously reported that a *C. utilis* strain lacked acid trehalase, but could grow in trehalose medium. Thus it was assumed that in this *C. utilis* strain, neutral trehalase had an important role in extracellular trehalose utilization. We were interested in studying the only trehalase enzyme present in *C. utilis*.

The neutral trehalase of *C. utilis* has been purified to homogeneity as evidenced by electrophoretic and chromatographic means. The enzyme is found to show a single band in SDS-PAGE. The N-terminal amino acid sequencing of the single protein band revealed that the enzyme is a novel protein. Chromatographic data, SDS-PAGE and analytical ultracentrifugation data indicate that the active enzyme is a tri-mer of a 56 kDa polypeptide. Different char acterization protocols have also been carried out to show that the enzyme has characters partially similar to both acid trehalase and neutral trehalase of *S. cerevisiae*.

Chemical Standardization and Biological Evaluation with a view to Increase Efficacy of Herbal Medicines: Bioefficacy and Analytical Evaluation (Antimicrobial activity) Itone Eye Drops (CLP 214)

Itone is a poly herbal eye drop consisting of 21 herbs and spices. It contains 0.01% (w/v) benzalkonium chloride and 0.05% (v/v) phenylethyl alcohol as preservatives. Earlier we have shown that Itone consists of some essential oils; among them three oils namely eugenol, carvacrol and camphene were identified. In an attempt to find the microbicidal activity of Itone, antimicrobial assay was performed by measuring the growth of two types of microorganisms, yeast and bacteria, in the presence and absence of the test materials. Two yeast strains, *Saccharomyces cerevisiae* and *Candida utilis* and two Gram-positive bacterial strains, *Staphylococcus aureus* and *Bacillus cereus* were used in this study.

The minimum inhibitory concentration (MIC) for both the yeast strains was found to be 40% (v/v) Itone. In case of bacterial strains, 5% (v/v) Itone was found to be the MIC for S. aureus and 3.5% (v/v) for B. cereus respectively. It was 40% (v/v) Itone without preservatives that was found to be the MIC for both the yeast strains.

The anti yeast activity of different individual ingredients present in Itone with preservatives were tested on these two strains. It was found that 40% (v/v) distillate of 'Yamini' and 'Haridra' was the MIC for both the yeast strains. The distillate of 'Pudina' showed MIC at 40% (v/v) for C. utilis and 35% (v/v) for S. cerevisiae. The distillate of individual ingredients without preservatives did not produce any significant anti yeast activity.

Standardization and Identification of ingredients present in 'Trasina'. The amount of total sugar and glucose present in Trasina were determined and it was observed that the individual values varied significantly from batch to batch, but the total sugar - glucose ratios did not vary so much. The company was intended to provide an electron beam irradiation for sterilization of Trasina. It was observed that such electron beam irradiation had no effect on total sugar and glucose quantities. By doing High Performance Thin Layer Chromatography (HPTLC) in Trasina, oleanolic acid, which has anti-tumour activity along with different healing property, was identified and quantified. It was also observed that Tulsi, which is one of the ingredients of Trasina (major), is the sole source of oleanolic acid. By doing High Performance Liquid Chromatography (HPLC) S-Adenosyl L-Methionine (AdoMet), which is well known for its anti stress and anti aging activity was identified and quantified present in Trasina. It was also found that Aswagandha which is another ingredient of Trasina was the rich source of AdoMet.

Molecular mechanisms regulating production and secretion of carbohydrases in the fungus Termitomyces clypeatus

Dr. (Mrs.) Suman Khowala and group

Filamentous fungi are preferred over bacterial and mammalian systems due to their capacity to produce and secrete high amount of proteins/enzymes. Production of the proteins is influenced by several factors, but their release in extracellular milieu is known to be spontaneous. In the filamentous fungus *T. clypeatus* regulatory secretion of proteins is identified and reported. Studies are being carried out to understand the regulatory control of production and secretion of glycosidases using cellobiase from filamentous fungus *T. clypeatus* as a model enzyme.

Insights into the secretory traffic. We studied both the effect of induction of secretory stress on cellobiase, a model secretory fungal glycosidase of our lab, as well as the associated physiological changes. Brefeldin A, a fungal macrocyclic lactone, disrupts secretory traffic by blocking transport of COP I coated vesicles from ER to cis Golgi. Fungal cultures were treated with Brefeldin A (50 µg/ml) to block sorting of secretory proteins and subsequently to induce secretory stress. The Spitzenkorper, (a dense cluster of secretory vesicles at the hyphal tip responsible for both nutrient uptake by endocytosis and secretion of enzymes & other metabolites by exocytosis) got disrupted in presence of Brefeldin A, as evidenced by FM 4-64 dye uptake in live fungal hypha (Fig. 17A & 17B); a parallel culture grown under unfavorable secreting conditions, where there is a marked decrease in turnover of vesicles and a consequent reduced growth, was also subjected to the dye uptake under similar conditions. In this case weak fluorescence confined at the hyphal tip (Fig. 17C) proved that dye uptake is not random but occurs only through vesicular endocytosis at the hyphal tip. Concomitant with the disruption of the Spitzenkorper, there was a fall in total cellobiase synthesis and overall reduced growth, by about 50% in presence of the drug. Organization of the Endoplasmic reticulum was also disrupted severely (Fig. 18A & 18B). However, the extracellular secretion of cellobiase with respect to distribution of total cellobiase units in three different cellular milieus (extracellular, cell bound & intracellular) remained unaltered. Glycosylation content of the enzyme remained unchanged in presence of the drug. This suggested the sorting of cellobiase through the secretory pathway via Golgi independent alternate route. The results show important lead about regulation of secretory pathway in the fungus in the background of the significant role of glycosylation already observed on the activity and secretion of the cellobiase.

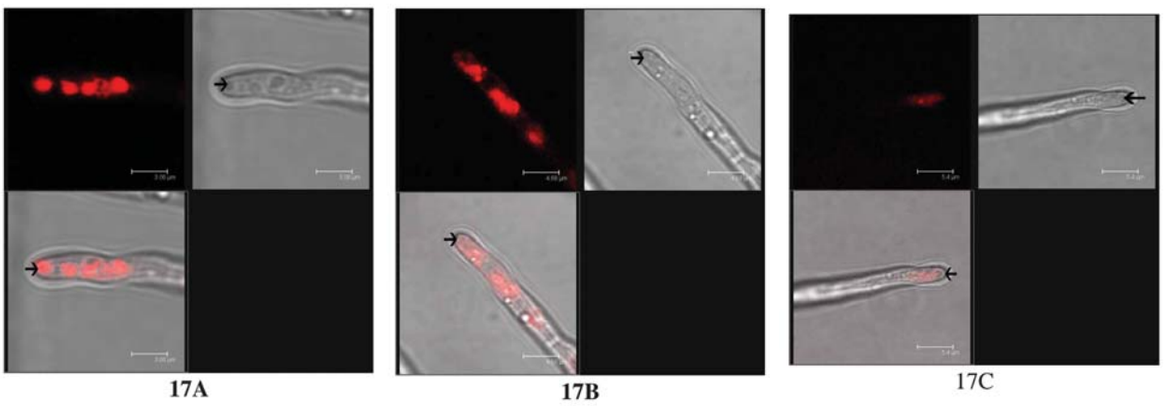
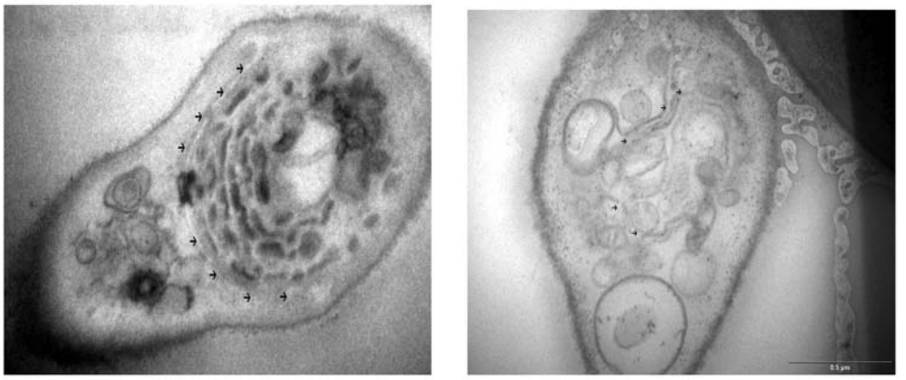


Fig. 17. Brefeldin A disrupts Spitzenkorper assembly in filamentous fungi. Fluorescence confocal microscopy of control hyphae showing distinct *Spitzenkorper* localized at the tip **(17A)**; Hyphae grown in presence of BFA with disrupted *Spitzenkorper* at the tip barely visible **(17B)**; Hyphae grown under non-secreting conditions show weak fluorescence at the hyphal tip **(17C)**.



18A 18B

Fig. 18. TEM image of hyphal cross section. 18A, well organized ER (control); **18B**, disrupted ER (treated with brefeldin A)

Regulatory effects of glycosylation inhibitors. Significant changes in activity and secretion of cellobiase and protein were observed in the fungus in presence of glycosylation inhibitors e.g. 2-deoxyD-glucose (DG). Tunicamycin (TN), deoxy-nozirimycin (DN) and D-Glucono-lactone (GL). Enzyme activity increased by 30-40 times by adding DG and protein synthesis was also high by 20% in the medium. Total cellobiase activity increased by the inhibitors in general; activity was more than double in presence of DN. on Total protein secretion increased to ~95% and synthesis reduced by 25% in presence of TN and DN, and cellobiase secretion was only approx. 40% in comparison to 71% of control culture. In presence of GL significant enzyme activity (55%) and protein (40%) retained in cell bound fractions. (Biotecnology Letters 28, 1773-1778, 2006). Post-translational modification by glycosylation had significant regulation on production, activity & secretion of enzyme and proteins in the fungus.

Co-aggregation of sucrase. Earlier detection of sucrase in co-aggregation with cellobiase was shown to affect activity and secretion of the enzyme, where segregation of sucrase from the aggregate led to lowering of enzymic activity of sucrase and cellobiase as well. Recently, results showed that addition of purified sucrase into cellobiase led to regain of 25-30% of sucrase activity. Purified sucrase was also characterised for physicochemical properties and results were different from those of the co-aggregates at different stages of purification.

Medicinal plants and metabolic engineering

Dr. Sharmila Chattopadhyay and group

Natural antioxidants are in high demand not only for its use as neutraceuticals but also for its pharmaceuticals value. At least two major human problems, cancer and aging, involve ROS mediated DNA damage and plants rich in biologically active phytochemicals play a vital role in prevention. Present study has been framed with an endeavor to identify new phytotherapeutic agents from commonly used plants. We investigated Pudina extracts for their oxidative DNA damage preventive activity and antioxidant potential. Our results showed that the bioactive fraction is highly effective compared to other plant extracts (Table 3). It also showed significant preventive activity against DNA strand scission by °OH on pBluescript II SK (-) DNA as reflected through densitometric analysis.

Genetic modification of model (*Nicotiana tabacum*) and target (*Mentha arvensis, M. piperita*) plants was created in order to obtain qualitative and/or quantitative enhancement of desired secondary metabolites of pharmaceutical interest. Glutathione, the cell's master antioxidant was targeted to be enhanced by the overexpression of γ-ECS, the key enzyme of GSH pathway. The coding sequence of γ-ECS was cloned in a binary vector, pBI121

and transform in tobacco and Pudina. The integration and confirmation of the markers and the gene of interest in transgenic lines, as regenerated true to mother type (Fig. 19), was confirmed by PCR, Southern-blot & RT-PCR (Fig. 20).

Table 3. Antioxidant potential of some useful plants

Name of plants	ROS scavenging activity (µg/ml)			DNA Damage Preventive Activity [b](µg/ml)
	ABTS[a]	DPPH[a]	°OH[a]	
Pudina	8.8±0.75	16.6±0.63	12±1.56	10±2.1
PA 202	40±1.35	250±2.57	80±0.75	500±3.5
SR 51	10±0.38	18.6±0.34	10±0.87	100±1.63
NA 101	20±0.58	42±1.73	33±0.58	180±1.20

[a]Indicating the concentration that conferred 90% scavenging activity against ROS.
[b]DNA damage preventive activity as noted in Densitometric analysis (BIORAD Quantity One).

19A

19B

Fig. 19. Regeneration of complete transgenic plants (19A & 19B).

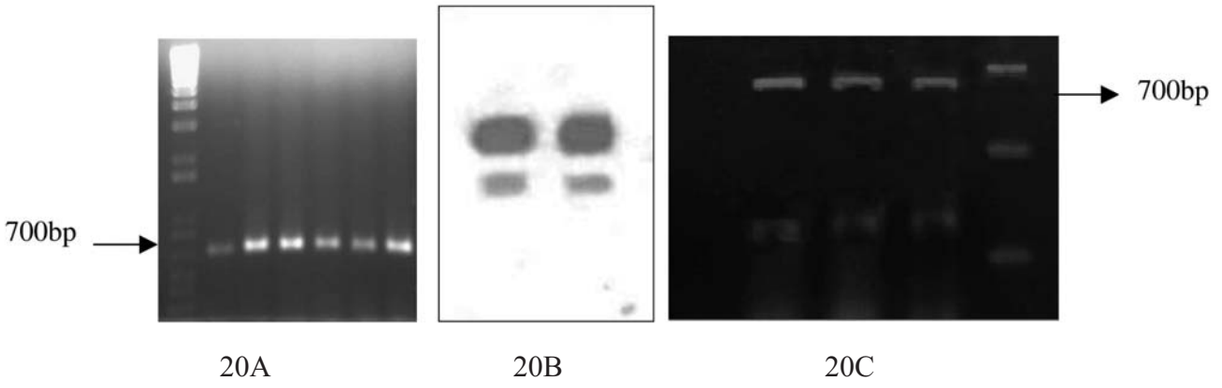


Fig. 20. Molecular analysis of transgenics (20A, 20B & 20C).

Technical staffs

Dr. (Mrs.) Shila E. Besra, Dr. Ramdhan Majhi, Dr. Ardhendu K. Mandal, Mrs. Dipika Roy, Mr. M. L. Jana.

RAs etc.

Dr. (Mrs) Mrinalini Bhattacharya, Dr. (Miss) Neela Sen Gupta, Dr. Kausik Mazumder, Dr. Rina Saha, Dr. (Mrs) Anamika V. Sharma.

Research Fellows

Dr. (Mrs). Papiya Ghosh, Debopam Acharya, Debjani Saha, Ruplekha Chatterjee, Dhananjoy Soren, Sharmishtha Mazumder, Tanima Saha, Debannita Dutta, Arghya Basu, Paramita Chaudhuri, Parag Kundu, Krishnendu Ganguly, Sumit Paul, Laishram Pradeep Singh, Anindita Debnath, Shubho Dasgupta, Anindita Banerjee, Amrita Chakraborty, Srijani Ghanta, Dipto Bhattacharya, Avijit Poddar, Suchandra Goswami, Ms. Chinniah Annalakshmi, Sudip K. Kar, Sudeshna Chowdhury, Shakuntala Ghorai, Swagata Pal, Samudra Prosad Banik.

Project Assistants

Dipankar Malakar, Anindya Dey, Nidhi Sharma, Amartya Mishra, Soma Roy, Sumana Mallick.

Summer Trainees

Kaushik Bhar, Subhasis Das, Soumendu Das, Abhideep Das, Sagar Lahiri, Sanjukta Das, Chitrita DuttaRoy, Mithun Chakraborty, Shilpi Gupta, Rajeeb Mazumdar, Jaspreet S Grewal

Chemistry

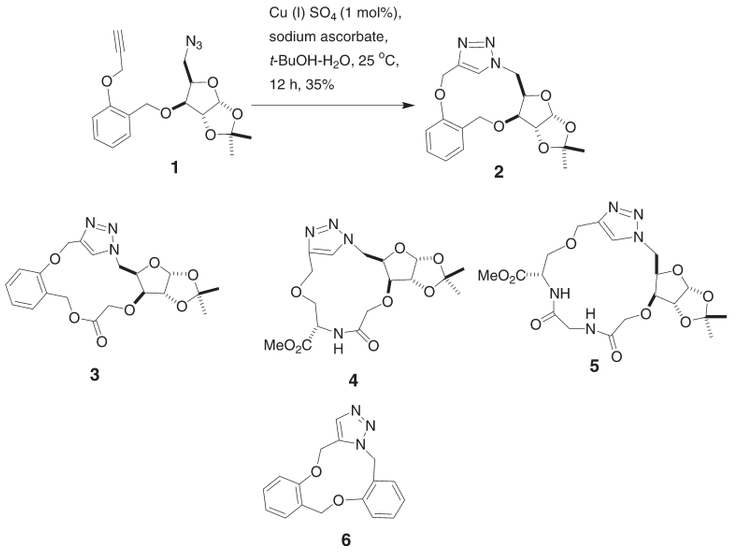
Drs. A. Bhattacharjya, V. S. Giri, S. B. Mandal, A. K. Sen (Sr.), P. K. Bhattacharya, Ajoy K. Banerjee, B. C. Pal, A. K. Sen (Jr.), S. Mukhopadhyay, P. Chattopadhyay, S. Bandopadhyay, G. Suresh Kumar, N. B. Mandal, B. Das, P. Jaisankar, R. Mukhopadhyay, Ashis K. Banerjee, R. C. Yadav, Chinmay Chowdhury and Arindam Banerjee

Over the years both synthetic as well as natural product chemists have been interested in the studies of secondary plant metabolites because of the interesting biological properties and also the complex structural features possessed by them. The major areas in which work has been carried out by investigators of the division in the recent past includes synthesis of chiral heterocycles, synthesis of novel nucleosides, synthesis of benz-annulated medium size rings, synthetic studies on heterocyclic chemistry, novel synthetic routes (enantioselective) to natural products, synthetic studies in homogeneous and organised media, synthesis of anti-leishmanial compounds, studies in bacterial cell surface antigens, plant polysaccharides and neoglycoproteins, chemical investigation of medicinal plants for bioactive substances and nucleic acid polymorphism. The chemistry division has also been engaged in some important collaborative industrial projects and has been successful in establishing a link with few established pharmaceutical industries .

Synthesis of 12 to 17-membered monomeric triazolophanes by Cu (I) catalyzed cycloaddition of azidoalkynes

Dr. Anup Bhattacharjya, Dr. R. Mukhopadhyay and group

Cycloaddition of constrained azidoalkynes incorporating furanoside rings in the presence of Cu(I) salts was studied. As an example, cycloaddition of **1** gave rise to the 12-membered triazolophane **2** in 35% yield (Scheme 1), which represents the first example of a 12-membered triazolophane. Similarly were synthesized the triazolophanes **3**, **4** and **5** from the corresponding azidoalkynes. Interestingly, in contrast to the usually observed regioselectivity in Cu(I)-catalyzed cycloaddition, the 1,5-disubstituted triazole **6** and, not the1,4-disubstituted isomer, was obtained by the Cu(I)-catalyzed cycloaddtion of the corresponding azidoalkyne. The structure of 6 was established by X-ray diffraction analysis.



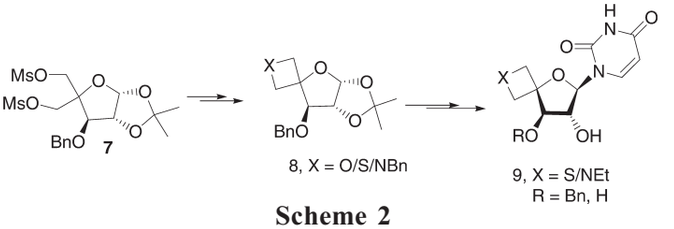
Scheme 2

Synthetic approaches to structurally novel chiral nucleosides and analogues from D-glucose

Dr. S. B. Mandal and group

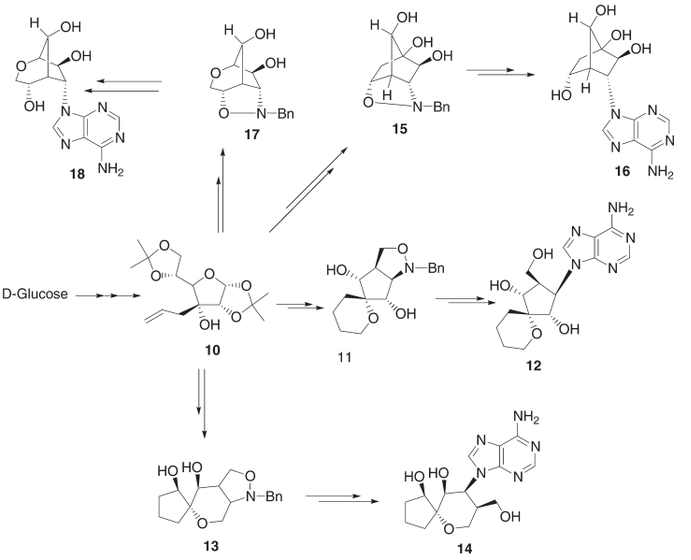
Exploitation of the backbone of commercially available carbohydrates for developing methods for the synthesis of important chiral molecules continues unabated. The principal objective of the subproject is to develop synthetic routes to structurally unique nucleosides and analogues from D-glucose derived precursors.

Spironucleosides with oxetane, thietane and azetane rings. The key intermediate **7** derived from D-glucose and possessing bis-mesylmethyl ($MsO.CH_2$-) functionality at C-4, was used to generate spirocycles **8** via one-step procedures. The spiro compounds **8** were subsequently converted into the corresponding spironucleosides **9** (Scheme 2) in good yield using Vorbrüggen reaction conditions.



Scheme 2

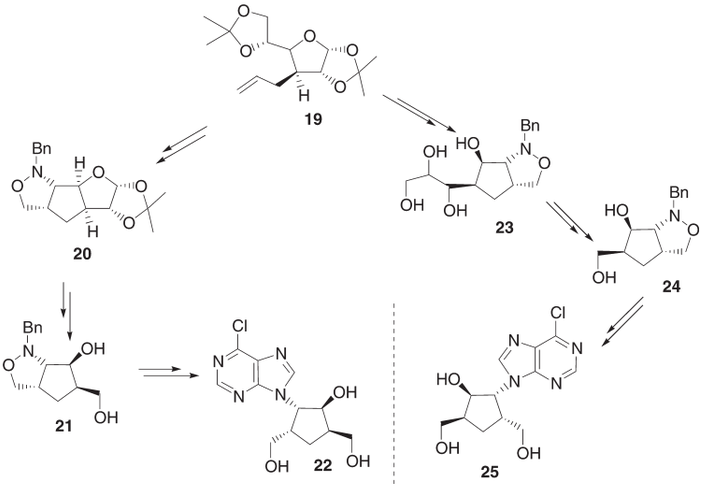
Spiroannulated carbanucleosides and conformationally locked nucleosides. The carbohydrate derived substrate 3-C-allyl-1, 2:5, 6-di-O-isopropylidene-(-D-allofuranose (**10**) was judiciously manipulated for preparing suitable synthons which could be converted to a variety of isooxazolidino-spirocycles **11** and **13** and -tricycles **15** and **17** through the application of ring closing metathesis (RCM) and intramolecular nitrone cycloaddition (INC) reactions (Scheme 3). Cleavage of the isooxazolidine rings of some of these derivatives by tranfer hydrogenolysis followed by coupling of the generated amino functionalities with 5-amino-4, 6-dichloropyrimidine furnished the corresponding chloropyrimidine nucleosides, which were elaborated to spiroannulated carbanucleosides **12** and **14**, and conformationally locked bicyclo [2.2.1] heptane/oxa-bicyclo[3.2.1] octane nucleosides **16** and **18**.



Scheme 3

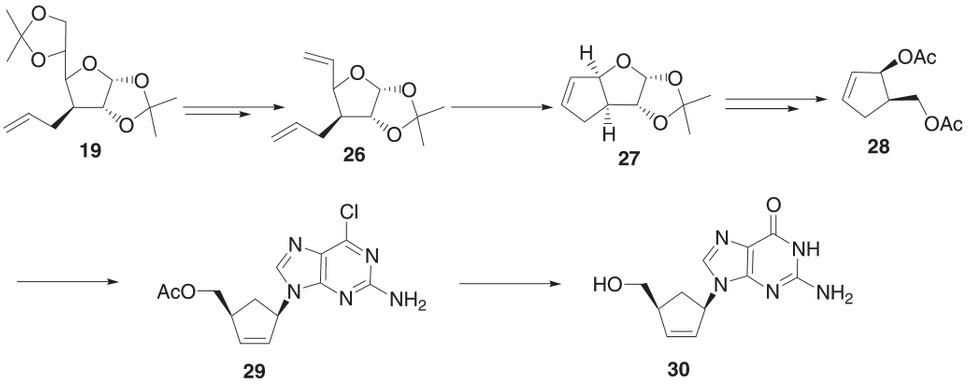
Enantiodivergent synthesis of carbanucleosides. D-Glucose derived key intermediate 1, 2:5, 6-di-O-isopropylidene-3-deoxy-3ß-allyl-β-D-glucofuranose (**19**), conveniently prepared through radical induced allyl

substitution at C-3 of appropriate 1, 2:5, 6-di-O-isopropylidene-α-D-glucofuranose derivatives was used to synthesize enantiomeric bishydroxymethyl aminocyclopentanols **21** and **24** (via the intermediates **20** and **23**) by application of a 1,3-dipolar nitrone cycloaddition reaction involving the C-5 or C-1 aldehyde functionality. The products were subsequently transformed to the carbanucleoside enantiomers **22** and **25** (Scheme 4).



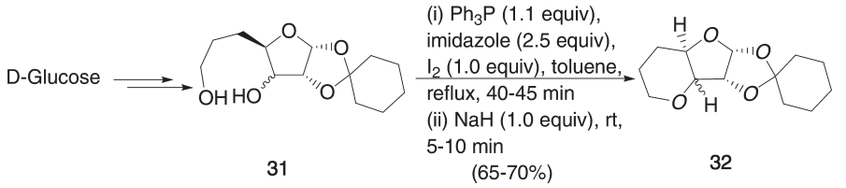
Scheme 4

Synthesis of (-)-carbovir. Selective removal of the 5,6-O-isopropylidene group of **19** followed by olefination provided the diolefin **26**, which upon RCM reaction furnished the cyclopentene fused furan **27** (Scheme 5). Opening of the 1,2-acetonide of **27**, vicinal diol cleavage, $NaBH_4$, and subsequent acetylation of the diol (5-hydroxymethyl-cyclopent-2-enol) yielded the desired diacetate **28**. Palladium-catalyzed coupling of **28** with 2-amino-6-chloropurine produced the purine carbanucleoside **29**, which was hydrolyzed with aqueous sodium hydroxide to furnish carbovir **30**.



Scheme 5

Methodology for cyclic ethers. A novel and efficient one-pot cyclization method using triphenylphosphine, iodine and a nitrogenous base has been established for the synthesis of cyclic ethers of various ring sizes (Scheme 6). As for example, the diol **31** was converted to **32**. This appears to follow a two-step procedure, which includes preferential substitution of one hydroxyl group by iodide generated *in-situ* followed by an intramolecular ring closure through the attack of a free hydroxyl group or the more nucleophilic oxide ion. These bicyclic ethers are the precursor for many bioactive nucleosides.



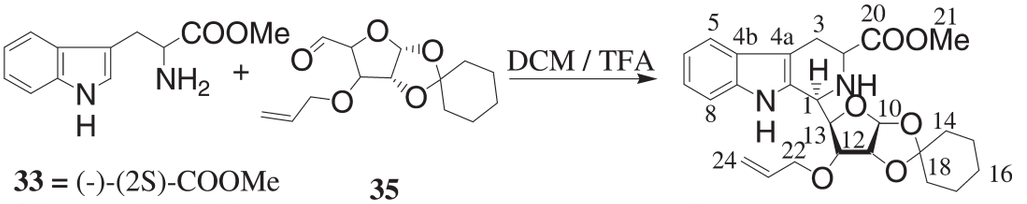
Scheme 6

Further study of this subproject will involve synthesis of new classes of bio-active nucleoside by the application of appropriate reactions on carbohydrate skeletons.

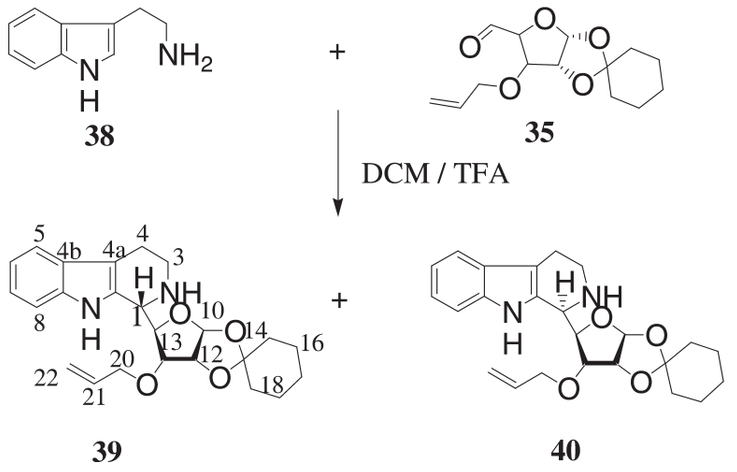
Synthetic studies in heterocyclic chemistry

Dr. Venkatachalam Sesha Giri, Dr. Parasuraman Jaisankar and group

Recently we have made an important observation that when Pictet-Spengler reaction of L- or D- tryptophan methyl ester (**33** or **34**) was performed with 1,2-*O*-cyclohexylidine-3-allyloxy-α-D-xylopentoaldo furanose **(35)**, only one product (**36** or **37**) was obtained (Scheme 7) although reaction with tryptamine **(38)** under the same condition afforded the diastereomers **39** and **40** (Scheme 8).

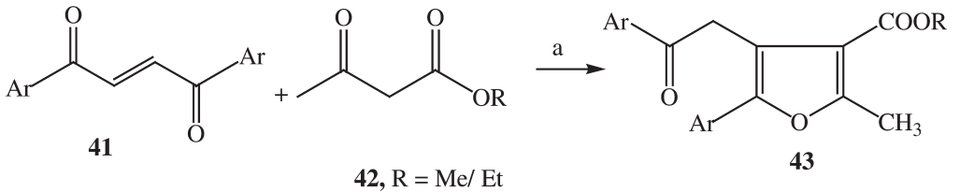


Scheme 7



Scheme 8

A one-pot synthesis of the substituted furans **43** could be achieved (Scheme 9) in good yields by reacting but-2-ene-1,4-diones **41** with acetoacetates **42** in the presence of a catalytic amount of $InCl_3$ (20 mol %) using i-PrOH as solvent at 80-90°C for 4-8 h. $InCl_3$ was observed to give the optimum results among the various Lewis acids examined.



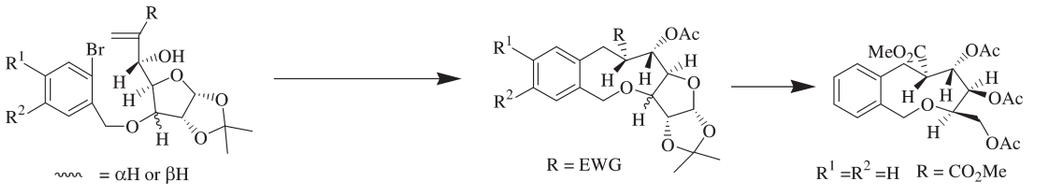
Reagents and conditions: (a) $InCl_3$ (20 mol%), *i*-PrOH, reflux at 80-90 ^oC.

Scheme 9

Synthesis of annulated medium ring heterocycles

Dr. Partha Chattopadhyay and group

The broad objective of this subproject is to develop synthetic methodology for medium ring ethers or analogues possessing diverse biological properties. In continuation of our previous studies on the synthesis of bezofused medium ring heterocycles (present in drugs or many biologically active product), radical cyclization has been accomplished on various sugar-derived intermediates. Compared to benzoxepines or benzoxocines, synthetic routes to benzoxonine rings are scare. We had earlier reported successful preparation of the benzannulated seven- and eight- membered oxacycles through radical cyclization on unsubstituted olefins. Unfortunately, this method could not be extended to the synthesis of nine membered ring systems despite repeated attempts with variations in reagent or condition. We, therefore, envisaged that the presence of an electron withdrawing group conjugated to the olefinic bond might help the ring closure by 1,4 addition, leading to the formation of the desired ring system. Thus, starting from our carbohydrate derived chirons suitably designed Baylis-Hillman adducts could be accessible using appropriate acrylates and acrylonitrile in the presence of DABCO in dioxane-water. Subsequently, it underwent TBTH-AIBN mediated intramolecular radical cyclization in 9-endo-trig pathway to the enantiopure benzoxonine derivatives (Scheme 10). The stereochemistry of most of the oxonine derivatives could not be established by 1H NMR spectroscopy due to their poorly resolved spectra. However the structure was determined by X-ray diffraction study (Fig. 1). The reaction worked on a variety of D-glucose derived substrates and explored to D-allose derived products.



Scheme 10

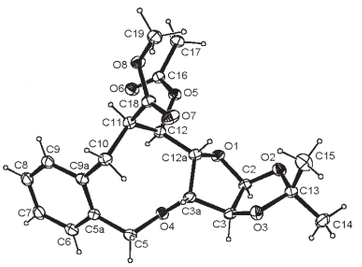


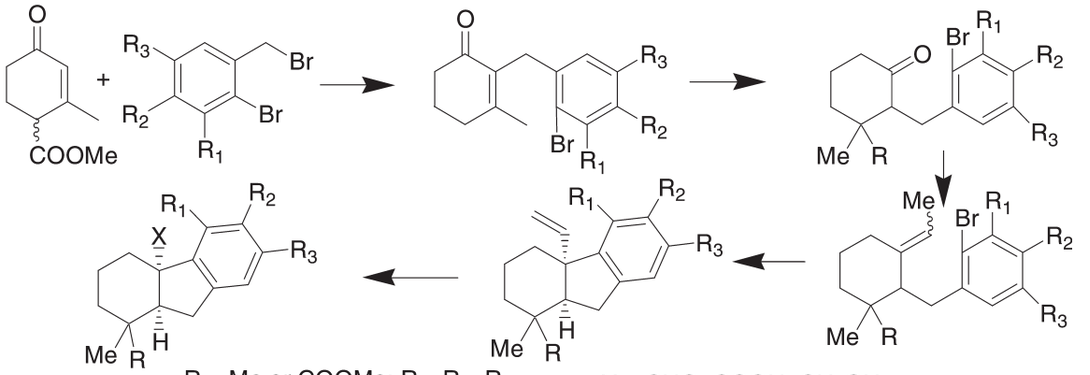
Fig. 1

Novel synthetic routes for natural products–enantioselective approaches and radical cyclization strategies

Dr. Asish Kr. Banerjee and group

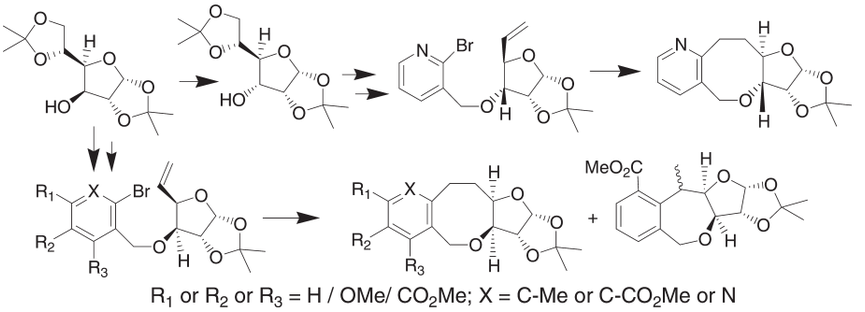
The sub-project aims at establishing novel strategies for the synthesis of terpenoid natural products, developing stereoselective synthetic methodologies, and application of regioselective radical reactions for the construction of condensed carbo- and heterocyclic ring systems. Hydrofluorenes constitute the basic skeleton of a large number of highly functionalized diterpenoids of the gibberellin and rearranged abietane groups. An efficient and high yielding methodology based on Pd (0)-mediated Heck cyclization has been developed for the synthesis of 4a-vinyl-1-substituted hydrofluorenes, models towards gibberellins and other rearranged abietane diterpeniods.

The required bromobenzyl substituted ethylidene cyclohexane substrates were conveniently derived from Hagemann's ester (Scheme 11). Simple organic transformations converted the vinyl group in the Heck cyclization product to carboxy, formyl or hydroxymethyl group. The ring juncture stereochemistry of the products was established through correlation approach.



Scheme 11

Earlier, we have described the application of intramolecular tributyltinhydride mediated radical cyclization to prepare fused five to nine membered fused pyridine ring systems. Using this strategy, intramolecular radical cyclization studies using variously substituted aromatic glucofurano-olefinic substrates as well as 2-bromopyridyl glucofurano- and allofurano-olefinic substrates gave the evidence for the mode of ring closure in the carbohydrate derived olefins. High endo-selectivity resulted when an electron-withdrawing group was present para to the generated radical or when a heteroatom was present at the ortho position. Low selectivity was observed when either an electron donating or electron-withdrawing group was present ortho or meta to the generated radical. The above experiments also describe a new approach to the formation of new cis- and trans-pyrido fused tricyclic chiral ethers (Scheme 12).



Scheme 12

Synthetic studies in homogeneous and organised media

Dr. P. K. Bhattacharya and group

A highly stereoselective surfactant-catalyzed intramolecular nitrone (formed by dehydration in water) cycloaddition in aqueous media leading to exclusive formation of a single isomer has been reported. Either oxepane or pyran is formed from 3-O-allyl furanoside derivatives, which constitute the framework of a large number of biologically active compounds. Therefore, the environmentally friendly, efficient, and highly stereoselective syntheses of these chiral intermediates are still a meaningful pursuit.

Synthesis of antileishmanial compounds

Dr. N. B. Mondal, Dr. Sukdeb Banerjee and group

Our continued search for antileishmanial chemotherapeutic agents yielded 2-(2-methylquinolin-4-ylamino)-N-phenylacetamide (S-4) as a lead molecule. Acute and sub-acute toxicity studies (at IIBAT, Chennai, Tamilnadu) revealed that the molecule is nontoxic. A number of analogues of the lead molecule have been synthesized and evaluated for antileishmanial efficacy; both *in-vitro* and *in-vivo* against *L. donovani* strain AG83. An Indian Patent has been applied. A simple and one pot methodology has been developed for the synthesis of 1,4-diphenyl piperazine 2,5-dione (Fig. 2, DKP). A number of DKP's have been synthesized and evaluated against *Leishmania donovani* strain AG83. From this evaluation, one compound (1,4 dicyclohexyl piperazine 2,5-dione) has emerged as the most effective; *in-vitro* studies revealed its efficacy to be equivalent to that of pentamidine, the standard antileishmanial drug. Simultaneously, the development of methodology for the synthesis of expanded ring system of fused tricyclic 1,4-oxazinoquinolone under PTC catalysed conditions, iodine catalyzed synthesis of triindolyl methane (TRIM), and trinuclear oxindole analogues are in progress.

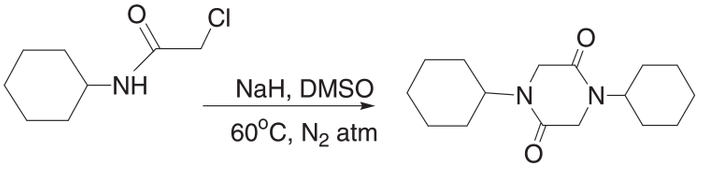


Fig. 2

Studies on bacterial cell surface antigens and medicinal plant polysaccharides and synthesis of neo-glycoproteins

Dr. Asish Kumar Sen (Jr.) and group

Structural studies on bacterial cell surface antigens. The objectives of this project are to isolate and elucidate the structures of the bacterial cell surface antigenic lipopolysaccharides (LPS) or polysaccharides (OPS) and capsular polysaccharides (CPS) from various pathogenic strains that are responsible for gastrointestinal diseases. The lipopolysaccharide from Vibrio parahaemolyticus O3:K6 has been isolated and purified. The LPS on mild acid hydrolysis produced the O-antigenic polysaccharide (OPS). This O-antigen, which is a decasaccharide, contains an unusual triamino sugar along with glucose, galactose and L-glycero-D-mannoheptose. Molecular weight of the OPS was found to be 1977 by MALDI-TOF. The structure of the triamino sugar has been established by COSY, TOCSY, HSQC and HMBC experiments. Detailed structural study on the OPS is in progress.

Synthesis of neo-glycoproteins. Synthesis of the immuno-dominant group (Fig. 3) of the O-antigenic polysaccharide of *Vibrio cholerae* O37 has been undertaken. Suitably protected donor and accepter molecules have been synthesized and the glycosylation and conjugation of the disaccharide with a suitable protein is in progress.

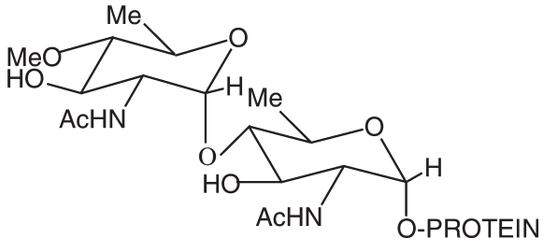


Fig. 3

Studies on medicinal plant polysaccharides. The constituent polysaccharides from Aegle marmelos (Bael) have been isolated using sequential extraction protocol. The neutral and acidic polysaccharides have been fractionated and partially purified. The acidic polysaccharide, isolated by hot water, showed significant anti-Leishmanial, and moderate anti-microbicidal activity. This acidic polysaccharide contains rhamnose, arabinose, galactose and glucose besides galacturonic acid. Further purification work is in progress for structural and biological activity studies.

Characterization and structural modification of coir fiber for enhanced longevity. The objective of this project is to modify the coir fiber chemically or by enzyme to protect them from degradation by light (UV). Before that it will be necessary to identify the type of compounds that are present on the surface of the coir fiber. The project has been sponsored by Coir Board from November 2006.

CHEMISTRY

Chemical investigation of medicinal plants for bioactive substances

Dr. S. Bandopadhya, Dr. N. B. Mandal and group

Three steroidal saponins, racemosides A, B, and C were isolated from the methanolic extract of the fruits of *Asparagus racemosus*, and characterized as (25S)-5β-spirostan-3β-ol-3-O-{β-D-glucopyranosyl (1→6)-[α-L-rhamnopyranosyl (1→6)-β-D-glucopyranosyl) (1→4)]-(-D-glucopyranoside}, (25S)-5β-spirostan-3β- ol-3-O-α-L-rhamnopyranosyl (1→6β-(-D-glucopyranosyl (1→6)-β-D-glucopyranoside, and (25S)-5β-spirostan-3β-ol-3-O{-α-L-rhamnopyranosyl-(1→6)-[α-L-rhamnopyranosyl(1→4)]-β-D-glucopyranoside} (Fig. 4) respectively, by spectro metric analysis and some chemical strategies. (Phytochemistry, *67*: 1316-1321, 2006).

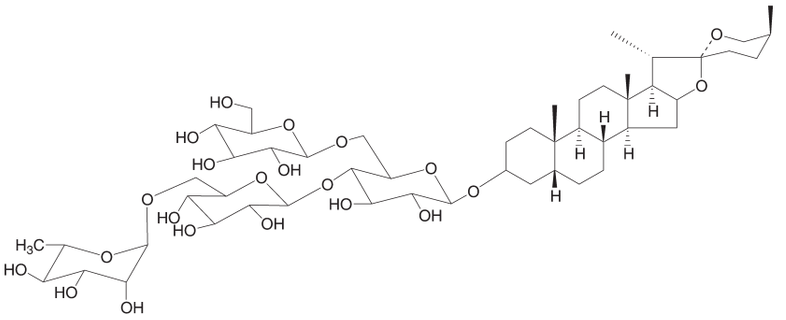


Fig. 4

Bassic acid (Fig. 5) isolated from *Mimusops elengi* was tested for its antileishmanial properties both *in vivo* and *in vitro* in hamster models of visceral leishmaniasis both in free form as well as incorporated in two different delivery systems, viz. microemulsions and polylactide nanoparticles. At an equivalent dose of 2 mg/kg body weight, when injected subcutaneously for a total of six doses in 15 days, bassic acid was found to reduce spleen parasite loads by 45, 62, and 78% in free, microemulsion-incorporated, and nanoparticle-incorporated forms

respectively. Because of its high efficacy as well as non-hepatotoxicity and non-nephrotoxicity, the nanoparticulate form of bassic acid may be considered for clinical application in humans rather than the microemulsion incorporated form. (Journal of Drug Targeting, *14*:171-179, 2006).

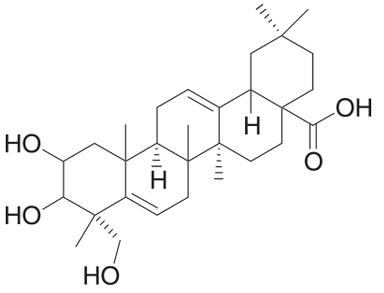


Fig. 5

Pregnane glycosides constitute a class of compounds widely distributed in the plant kingdom. Many of them have shown either anti-carcinogenic or cancer inhibitory properties, besides other useful biological activities. New chromatographic techniques and advances in spectroscopic and spectrometric methods have accelerated the purification and structure determination of novel glycosides of this series. A compilation of the pregnane glycosides isolated from 1995 until the middle of 2005, along with their physical data structures and occurrence are presented in a review, which also summarizes, with suitable examples, recent developments in isolation and purification techniques, and structural elucidation using modern spectrometric methods like ESIMS and tandem mass spectrometry and 2D NMR spectroscopic strategies. The reported anticancer and other biological activities of pregnane glycosides are also discussed. (Natural Product Communications, *1*: 665-695, 2006).

A new acylated flavone C-glycoside, dregeanin (Fig. 6), was isolated from the flowers of *Dregea volubilis*, together with vicenin-2, vitexin, isovitexin, isoorientin, rutin, quercetin, luteolin and apigenin. The structure was established by spectroscopic analysis as apigenin-{6-C-(-D-glucosyl-2"-O-feruloyl}-8-C-(-D-gluco-pyranoside (Natural Product Communications, *1*: 731-733, 2006).

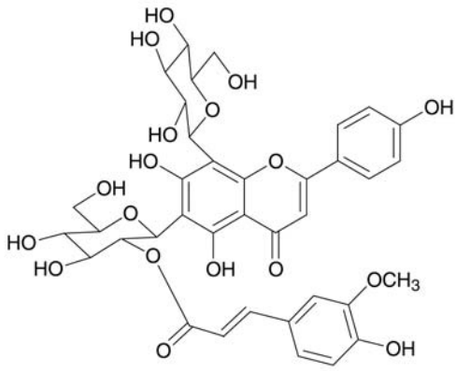


Fig. 6

X-ray crystallographic analysis revealed that farnesiaside (Fig. 7), a new diterpene glycoside with the acafarnane skeleton, consists of three cis-fused rings, of which the five membered ring is in an envelope conformation and the two six-membered rings adopt twist-boat and chair conformations. The lactone ring is in an envelope conformation. The D-glucose, in the β position with respect to the acafarnane skeleton, adopts a chair conformation. The molecular structure and the crystal packing are stabilized by O–H – – – O interactions including a bifurcated hydrogen bond. (Acta Crystallographica, *E62*: o4007-o4009, 2006).

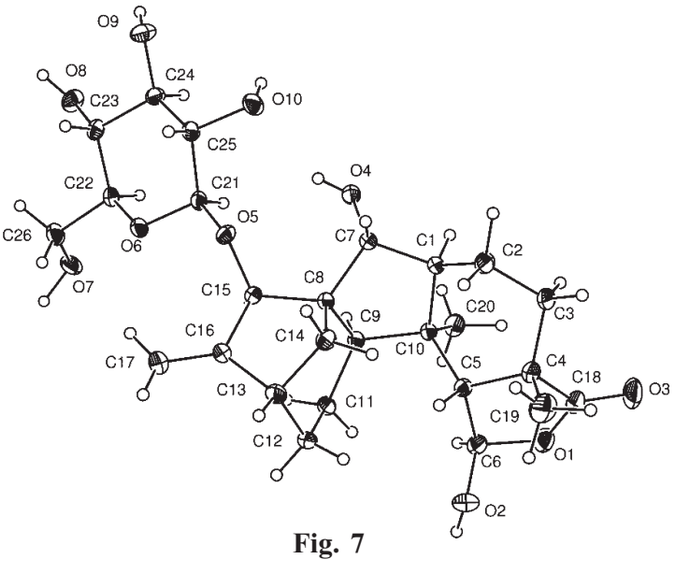


Fig. 7

The sperm-immobilizing and contraceptive potential of the aqueous extract of *Chenopodium album* seed has been evaluated in laboratory mammals. The mode of spermicidal action was assessed by (i) supravital and double fluoroprobe staining of sperm, (ii) hypoosmotic swelling test, and (iii) transmission electron microscopy, whereas contraceptive activity was assessed by intrauterine and vaginal application of the extract in rat and rabbits respectively, followed by their mating and evaluation of pregnancy outcomes. The MEC of the extract that induced instantaneous immobilization of rat spermatozoa in vitro was 2 mg/ml. The mechanism of action involved disintegration of sperm plasma membrane and dissolution of acrosomal cap causing sperm death. Fertilization of oocytes and establishment of implantation were prevented in the uterine horn that was treated with the extract, while the untreated horn showed no hindrance. In rabbit, intra-vaginal application of this extract significantly blocked the establishment of pregnancy. The results indicated that the extract might be explored as an effective constituent for vaginal contraception. (Contraception, *75*: 71-78, 2007).

Woodfordia fruticosa Kurz of the family Lythraceae is a plant of tropical and subtropical regions with a long history of medicinal use. A wide range of chemical compounds including tannins (especially those of macrocyclic hydrolysable class), flavonoids, anthraquinone glycosides, and polyphenols have been isolated from this species in recent times. Extracts and metabolites of this plant, particularly those from flowers and leaves, possess useful pharmacological activities. A comprehensive account of the chemical constituents and the biological activities has been presented in a review and a critical appraisal of the ethnopharmacological issues has been included in view of the many recent findings of importance on this plant. (Journal of Ethnopharmacology, *110*: 189-199, 2007).

The genus *Andrographis (Acanthaceae)*, widespread in nature, is frequently utilized for the treatment of various ailments in the Ayurvedic as also other indigenous systems of medicine. The occurrence of different chemical constituents from *Andrographis* genus, their spectral studies, biological activities, metabolism and also chemical transformations has been reviewed (see Under Books, Reviews etc.).

Dr. S. Mukhopadhyay and group (in collaboration with Dr. H. K. Majumder, Infectious Diseases group)

In continuation of our chemical investigation of *Andrographis paniculata Nees,* we have isolated a new labdane type diterpenoid, andropanolide along with several known diterpenoids and two flavonoids. Some of the isolated diterpenoids showed significant growth inhibitory effect on *L. donovani* promastigotes as well as amastigotes *in-vitro* and antileishmanial activity *in-vivo*, promoting topoisomerase mediated cleavage.

Our studies have indicated that leishmanial DNA topoisomerase is a potential target for anti-parasitic diseases. Search will continue to get more effective naturally occurring topoisomerase inhibitors which could become potential chemotherapeutic agents. Based on theses observations, search for new topoisomerase inhibitors from indigenous plants has been taken as the prime objective of this project.

Dr. Binayak Das and Group

Chemical investigation of the light petrol extract of the leaves of *Putranjiva Roxburgii* has led to the isolation of two new triterpenoids (putrone-10α-ol and an acetoxy derivative of a known triterpenoid) together with a number of known triterpenoids such as erythrodiol, putrol, putrone, roxburghonic acid, friedelin, freidelan-3α - ol. Further work on the MeOH extract of this plant is in progress. Moreoverr in the CSIR project entitled "Development & commercialisation of bioactive molecules from natural sources" extraction of Stem bark and leaves of Grewia asiatica were undertaken as per the extraction norms of CSIR and extracts obtained were sent to various sister CSIR laboratories for evaluation of bioactivity.

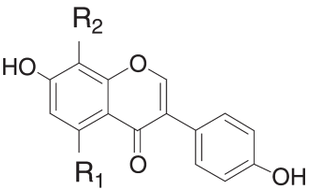
Dr. Chinmay Chowdhury and group

Our major interest has been to isolate and identify the bioactive chemical constituents from Indian medicinal plants. Towards this goal, sequencial fractionation of the methanol extract of the leaves of *Semecarpus anacardium* led to the isolation of interesting flavone glycoside besides some known molecules. The structure of the glycoside was established by COSY, TOCSY, HSQC and HMBC experiments. Further work is in progress to isolate novel compounds, characterise them and screen for their biological activity.

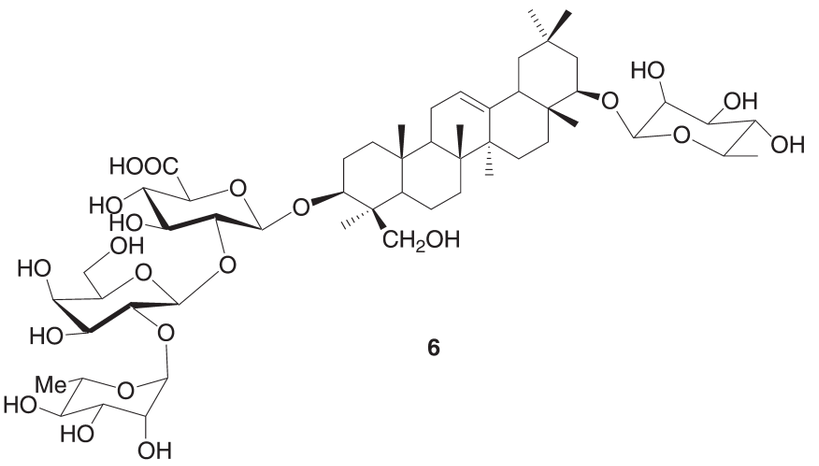
Development of herbal medicine

Dr. B.C. Pal and group (in collaboration with other groups)

In continuation of the research work on Type II anti-diabetic molecules further work was carried out on *Puereria tuberosa* root we have now isolated (Fig. 8) five isoflavones namely Daidzein **(1)**, Puerarin **(2)**, Genistein 8-C-glucoside **(3)**, Daidzein 8-C-apiosyl (1→6) glucoside **(4)**, Genistein 8-C-apiosyl (1→6) glucoside **(5)** and previously reported triterpenoid saponin, lupinoside PA4.**(6)**. Further research work on the development of bioactive medicinal plant is in progress.



	R_1	R_2
1.	H	H
2.	H	glucose
3.	OH	glucose
4.	H	apiose (1→ 6) β-D-glucose
5.	OH	apiose (1→ 6) β-D-glucose



6

Fig. 8

Nucleic acid polymorphic structures and their interaction with plant alkaloids

Dr. G. Suresh Kumar, Dr. R. C. Yadav and group

Molecular recognition of nucleic acids by alkaloids: Binding heterogeneity, conformational and thermodynamic aspects of binding of palmatine. In continuation of the work on molecular recognition of nucleic acid structures by alkaloids, the binding heterogeneity, conformational aspects and energetics of the interaction of the protoberberine alkaloid (Fig. 9) palmatine (a) have been studied with various natural and synthetic DNAs. The alkaloid binds to calf thymus and *Escherichia coli* DNA that have mixed AT and GC sequences in almost equal proportions with positive cooperativity while with *Clostridium perfringenes* and *Micrococcus leisodeikticus* DNA with predominantly high AT and GC sequences respectively, non-cooperative binding was observed. On further investigation with synthetic polynucleotides, the binding was observed to be cooperative with polymers poly (dA).poly(dT) and poly(dG).poly(dC) having poly(purine).poly(pyrimidine) sequences while with polymers poly(dA-dT).poly(dA-dT), poly(dA-dC).poly(dG-dT) and poly(dG-dC).poly(dG-dC) having alternating purine-pyrimidine sequences, a non-cooperative binding phenomenon was observed. This suggests the binding heterogeneity of palmatine to the two types of sequences of base pairs. A representative cooperative and non-

cooperative binding isotherm of palmatine is presented in (Fig. 10). Circular dichroic studies revealed that the binding induced conformational changes in all the DNAs, but more importantly, the bound alkaloid molecules acquired induced optical activity and the extent was dependent on the AT content and showed remarkable AT base pair specificity. Energetics of the interaction of the alkaloid studied by ultra sensitive isothermal titration calorimetry revealed that the binding in most cases was exothermic and favoured by both enthalpy and entropy changes while in case of the homo and hetero AT polymers the same was predominantly entropy driven. This study defines the unique base pair dependent heterogeneity, conformational aspects and energetics of palmatine binding to DNA.

Modulation of nucleic acid structural transition by alkaloid complexation: Induction of self structure in poly(A) by sanguinarine. Sanguinarine **(b)** is a quaternary benzo *[c]* phenanthridine alkaloid (Fig. 9) with wide range of potentially useful medicinal properties. Many of these medicinal properties have been suggested to be due to the interaction with nucleic acids that was shown for the first time from our laboratory to be intercalative and GC base pair specific. Sanguinarine, was now found to bind preferentially and strongly to single stranded poly(A) in comparison to several nucleic acids by competition dialysis. The large binding constant observed was in the range 3.6–4.6 x $10^6 M^{-1}$ that induced unique self-structure formation in poly(A) that showed cooperative melting transition in circular dichroism, absorbance, and differential scanning calorimetry studies. The alkaloid binding was characterized to be intercalation as revealed from fluorescence quenching experiments and was predominantly enthalpy driven as revealed from isothermal titration calorimetry. Sanguinarine **(a)** is the first and only natural product so far known to induce a self-structure formation in poly(A). This observation makes sanguinarine a promising lead compound for RNA based therapeutics.

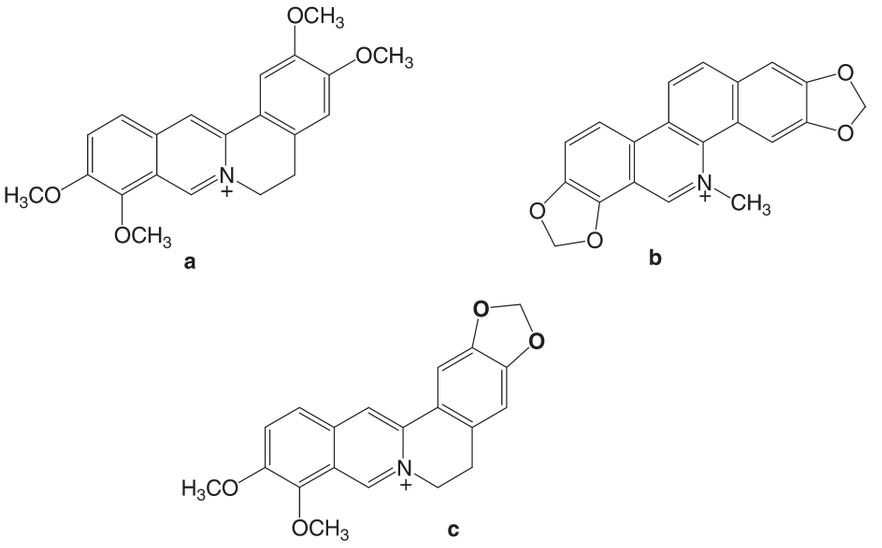


Fig. 9

Interaction of plant alkaloids palmatine and berberine with RNA. The binding affinity, energetics and conformational aspects of the interaction of isoquinoline alkaloids (Fig. 9), palmatine **(a)** and berberine **(c)** to four single stranded polyribonucleotides poly-guanylic acid [poly(G)], polyinosinic acid [poly(I)], polycytidylic acid [poly(C)] and polyuridylic acid [poly(U)] were studied by absorption, fluorescence, isothermal titration calorimetry and circular dichroism spectroscopy. Palmatine **(a)**, berberine **(c)** and ethidium binds strongly with poly(G) and poly(I) with affinity in the order $10^5 M^{-1}$ while their binding to poly(C) and poly(U) were very weak or practically nil. The same conclusions have also emerged from isothermal titration calorimetric studies. The binding of all the three compounds to poly(C) and poly(I) was exothermic and favored by both negative

enthalpy change and positive entropy change. Conformational changes in the polymer associated with the binding was observed in poly(I) with all the three molecules and poly(U) with ethidium but not in poly(G) and poly(C) revealing differences in the orientation of the bound molecules in the hitherto different helical organization of these polymers. These fundamental results may be useful and serve as database for the development of futuristic RNA based small molecule therapeutics.

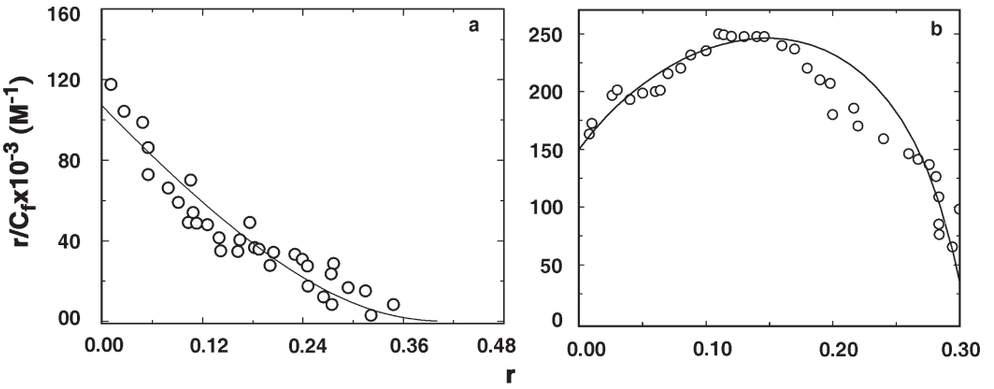


Fig. 10

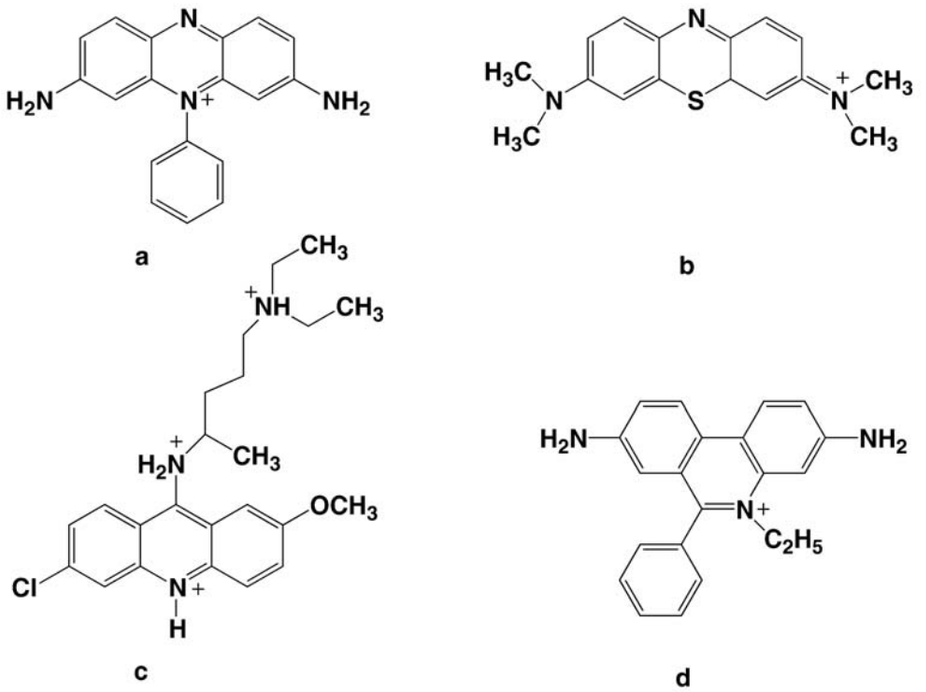


Fig. 11

Structural, conformational and energetic profiles of intercalative binding of small molecules in DNA. Various small molecules intercalate to DNA, but the functional groups and the structure of these molecules are different from each other. In order to understand the molecular aspects of structural heterogeneity in the interaction of various small molecules to DNA, a complete structural, conformational and thermodynamic profile of the

interaction of five known DNA intercalating molecules have been undertaken. The molecules chosen were (Fig. 11) phenosafranine **(a)**, methylene blue **(b)**, quinacrine **(c)** and ethidium **(d)**. Results reveal several unique and interesting features of interaction of these DNA intercalating molecules hitherto unknown. While phenosafranine, methylene blue and quinacrine bound to DNA by non-cooperative binding, ethidium revealed cooperative binding at very low inputs of the drug. While all these molecules intercalated classically to DNA obeying neighbour exclusion model, there were significant differences in the conformational and energetics of their binding that provided key significant insights into the role of various forces involved in the binding phenomenon. The differential binding affinities, structural aspects and energetics of interaction of these molecules to the DNA structure may provide key tools useful in the design of DNA based therapeutic agents.

Future programme of this sub project is to continue the study of RNA and DNA polymorphism in oligonucleotides and elucidate the specificity and energetics of interaction of natural and synthetic alkaloids, and other groove binding and intercalating compounds.

INDUSTRY SPONSORED PROJECTS

Identification and optimization of lead molecules for development as anti-cancer agents

Dr. V. S. Giri and Dr. A. K. Banerjee

This collaborative industrial project involving IICB, NCL, DRF with major grant from DST had its final monitoring meeting held at DRF, Sahibabad, UP, in the last week of May, 2006. It was suggested by the monitoring committee that in order to progress further a thorough pharmaco-kinetic properties of the lead molecules supplied by CSIR labs need to be done by DRF but appreciated the work done resulting in two international patents from IICB samples.

Indo-Poland Bilateral Research Programme - "Development of Chiral Catalysts for Asymmetric Organic Synthesis"

Dr. P. Jaisankar and group

Mutual visit under this bilateral research programme have been completed. The work is in progress to develop chiral catalysts for asymmetric transformation of various organic functional groups.

OPERATION AND MAINTENACE OF SOPHISTICATED INSTRUMENTS

Operation and maintenance of 600 MHz NMR Bruker spectrometer

Dr. Ranjan Mukhopadhyay and Mr. E. Padmanaban

The highly sophisticated 600 MHz Bruker NMR spectrometer has been maintained and analyses of about 600 samples were done during the year for both internal and external research workers. Apart from routine 1D experiments like PMR, PMR (HOD suppression), CMR, DEPT 135, DEPT 90, NOE difference and 2H-NMR various 2D and 3D experiments are being done regularly. 2D experiments include COSY, DQF-COSY, NOESY, NOESY-WG, TOCSY, TOCSY-WG, ROESY, HSQC, HMQC, HMBC, ADEQUATE and HSQCNOESY-15N. The 3D experiments mostly done are HNCOWG(13C/15N) and NOESYHSQC-15N.

Operation and maintenance of 300 MHz NMR Bruker spectrometer

Dr. V. S. Giri , Dr. Ranjan Mukhopadhyy and Dr. Tapas Sarkar

The 300 MHz Bruker DPX model NMR instrument has been extensively used during the year. About 2800 samples have been analyzed which includes both internal and external samples. 1D experiments mostly done are PMR, CMR (with DEPT 135 and DEPT 90), proton decoupling, NOE difference and variable temperature analyses. The 2D analyses routinely done includes COSY, NOESY, HMBC, HMQC, HSQC and COLOC experiments..

Operation and maintenance of Jasco 4200 FT/IR and Jasco 410 FT/ IR spectrophotometer

Dr. V. S. Giri and Dr. P. Jaisankar

The JASCO FT/IR 410 spectrophotometer has been routinely maintained and extensively used to analyse both internal and external samples. About 800 samples have been analyzed during the year. Samples are also routinely analysed in the recently procured JASCO 4200 spectrophotometer.

Operation and maintenance of LC-MS-MS-Q-TOF Micromass instrument

Dr. P. Jaisankar, Dr Asish K. Banerjee, Mr. Kalyan Kumar Sarkar and Mr. Diptendu Bhattacharya

One LC-MS-MS (Q-TOF Micor) instrument was installed in the middle of 2003. Since then it has been in use for routine mass spectral analysis of both internal and external samples. Small molecules as well as bio-macromolecules like proteins, carbohydrates etc. are being analyzed. Facilities include determination of their molecular weight, MS-MS experiments etc.

Jeol AX500 GC-mass Spectrometer

Shri Ajoy Banerjee (with operational support by Shri Sandip Chowdhury)

The Jeol AX500 Mass spectrometer is being routinely maintained by us and it is functioning well in different modes of analysis and is in use for the last sixteen years. Both internal and external (both academic as well industrial) researchers are making good use of the facility.

Gas liquid chromatograph

Dr. Asish K. Sen (Jr.)

Two Gas Liquid Chromatography instruments (Agilent 6890 plus and Hewlett-Packard 5890, fitted with FID detectors) have been maintained and samples are analyzed to cater to both in-house and external research workers including industries. During the year, ~250 samples have been analyzed which includes those of both internal and external users.

Shimadzu GC-mass spectrometer (GP5050 A)

Dr. B.C. Pal and Mr. A.K. Das

The GC-MS instrument is providing services to both internal and external research workers. About 250 samples have been analyzed during this year by Electron impact (EI), Chemical ionization (CI) and Direct inlet (DI) modes.

VP-ITC Model isothermal titration calorimeter

Dr. G. Suresh Kumar

An ultra sensitive Isothermal Titration Calorimetry Unit Model VP-ITC (Microcal, LLC USA) has been installed under the Central Instrumentation Facility for studying the thermodynamics of biomolecular interactions.

Jasco J720 spectropolarimeter

Dr. G. Suresh Kumar

The Circular Dichroism Unit is providing services to both internal and external workers. Solution conformation of peptides/proteins and nucleic acids are being routinely analyzed.

VP-DSC Model Differential Scanning Calorimeter

An ultra sensitive Differential Scanning Calorimetry Unit (Model VP-DSC, Microcal, LLC, USA) has been installed under the Central Instrumentation Facility for studying the thermodynamics of biomolecular interactions.

Biologic stopped flow accessory for the CD unit J715

A stopped flow accessory has been installed with the Jasco J715 CD spectropolarimeter

Emeritus Scientist

Drs. Basudeb Achari, P. K. Dutta, N. P. Sahu, Motilal Maiti

Technical Staff

Kalyan K. Sarkar, Asit Kumar Das, Subodh K. Roy, Sankar K. Maitra, Tapas K. Sarkar, Diptendu Bhattacharya, Gautam Gupta, Sandip Chowdhury, Sekhar Ghosh, Sarit K. Sarkhel, Rajendra Mahato, E. Padmanaban and Nimai C. Pradhan,

RAs and Research Fellows

Rangana Sinha, Mumu Chakraborty, Roshmi Roy, Abhijit Hazara, Amrita Chatterjee, Ankur Ray, Anupam Adhikari, Arpita Neogi, Ashim Roy, Biswajit Gopal Roy, Churala Pal, Debkumar Nandi, Gora Das, Goutam Biswas, Ishita Sanyal, Jhimli Sengupta, Joy Krishna Maiti, Kakali Bhadra, Koushik Mazumder, Madhumita Nath, Maidul Hossain, Mainak Banerjee, Md. Maidul Islam, Moumita Gupta, Nilendu Panda, Prabal Giri, Priyankar Paira, Ram Prasad Ghosh, Sandip K. Hota, Sarbendu Maiti, Seema Dutta, Scientist (WOS-A, DST), Shrabanti Kumar, Subir Ghorai, Sumit Dey, Swapan Pramanick, Tanmoy Biswas, Tirtha Pada Majhi, Subhrangshu Mukherjee, Prithwish Jana, Shinjini Bhattacharjee, Sohini Datta, Nirmal Das Adhikari, Krishnendu Bikash Sahu, Anup Kumar Sasmal, Raj Kumar Manna, Jewel Hossain, K. Dhanbal

Project Assistants

Prasun K. Pradhan, Sankar K. Dutta, Sudipta Saha, Sanjit K. Mahato, J. Vinayagam, Dipanjan Majumder

Summer Trainees

Sohani Das Sharma, Sritama Bose, Sreya Gupta, Moulisha Biswas, Himal Kanti Ganguly

Administrative Staff

Mr. Sankar Prasad Dutta, Sr.Stenographer

Structural Biology & Bioinformatics

Prof. Siddhartha Roy, Dr. M.C.Bagchi, Dr. Alok K. Datta, Dr. Chhabinath Mandal, Dr. Chitra Dutta, Dr. Debasish Bhattacharyya, Dr. Nanda Ghoshal, Dr. Soumen Datta, Dr. Krishnananda Chattopadhyay, Dr. Subrata Adak

Structural characteristics and conformational specificity to a large extent determine the mode of interaction between/or among all the biological macromolecules, leading to expression of their regulated functions. This institute has a long tradition of carrying out research on protein chemistry, molecular modeling of proteins, protein-nucleic-acid interactions, nucleic acid-drug interactions, and drug-protein interactions. Clearly, such structure-function studies require multi-pronged approach from different angles involving several areas of biological, chemical and physical sciences. Recently, we have undertaken an effort to bring all these disciplines under a common roof, resulting in the formation of the "Structural Biology & Bio-informatics" division. The charter of this division is to carry out research in areas that focus on structural characterization of potentially prospective biological macromolecules and other small molecules of therapeutic interest against various diseases, e.g. tuberculosis, leishmaniasis, cholera, cancer, diabetes and for other anti-inflamatory, anticonvulsant and immunomodulatory activities. Fundamental studies on protein functions, protein-protein and protein-nucleic acid interactions applying modern sophisticated technologies like nuclear magnetic resonance (NMR), X-ray crystallography, analytical ultracentrifuge, fluorescence correlation spectroscopy, diode array stopped-flow spectrophotometry, mass-spectrometry, quantitative structure activity relationship (QSAR) and 3D-QSAR are also being pursued. Softwares are being developed for genome / proteome analysis, prediction, modification and analysis of macromolecular structures and for elucidating their interactions with bio-active molecules.

Studies on macromolecular interactions and recognition

Prof. Siddhartha Roy & group

Understanding the nature of solvent molecules around proteins in native and different non-native states is crucial for elucidation of the protein folding problem. We have characterized two compact denatured states of glutaminyl-tRNA synthetase (GlnRS) under equilibraium conditions in the presence of a naturally occurring osmolyte, L-glutamate (Fig. 1). Solvation dynamics of the compact denatured states and the fully unfolded state has been studied using a covalently attached probe, acrylodan, near the active site. The solvation dynamics progressively becomes faster as the protein goes from native to molten globule to pre-molten globule intermediate is more flexible than the molten globule although the secondary structure is largely similar. Dynamic light scattering studies reveal that both the compact demantured state are aggregated under the measurement conditions. Thus, in pre-molten globule state, which is devoid of any organized tertiary structure, the solvation dynamics is slow, compared to the unfolded state. This idicates that even collapsed protein chains impose enough constraints to retard solvation dynamics, even in the absence of any organized tertiary interactions.

Fluorescence anisotropy decay. The decay of time resolved fluorescence anisotropy provides direct information on the oriental motion of a fluorophore in an organized assembly. The time-dependent fluorescence anisotropy, r(*t*), is given by

$$r(t))=[I_{II}(t) - GI_{\perp}(t)]/[I(t) + 2GI_{\perp}(t)]$$

where G is a correction factor for instrumental anisotropy. To study fluorescence anisotropy decay, the analyzer was rotated at regular intervals to obtain perpendicular ($I_{\perp}$) and parallel (I_{II}) components (Ïem= 450 nm). The G value of the setup was determined using a probe whose rotational relaxation is very fast, e.g., Nile red in methanol, and the G value was found to be 1. Anisotropy decay experiments of the probe acrylodan covalently

bound to GlnRS were done for the native, molten globule (3.5 M urea), pre molten globule (4.5 M urea), and unfolded (7.5 M urea) states in 0.1 M Tris-HCl, pH 7.5,containing 0.25 M L-Glu. HCl buffer, pH 7.5, containing 0.25 M L-Glu.

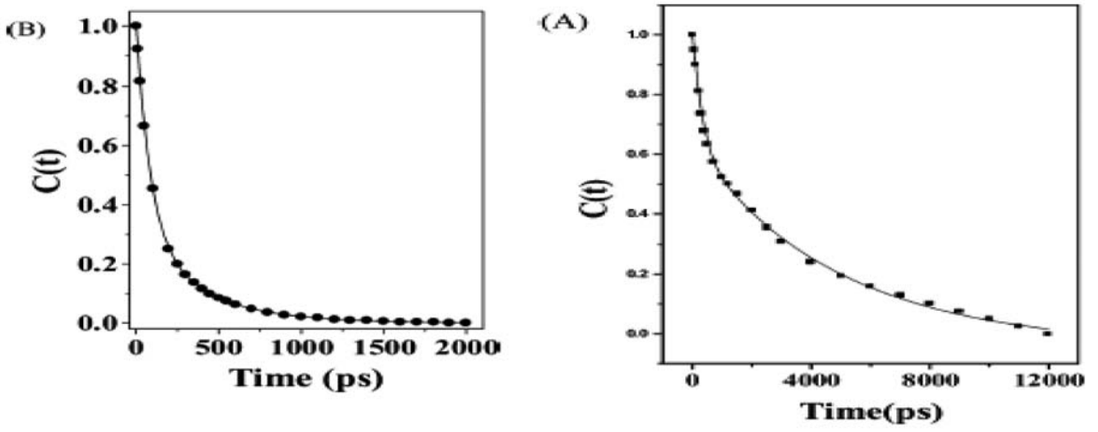


Fig.A **Fig.B**

Fig. 1 : Decay of the response function *C(t)* of acrylodan covalently bound to GlnRS. In the presence of 0.25 Ml-Glu in Tris-HCI buffer. pH 7.5, containing (A) 3.5 M urea and (B) 7.5 M urea. The points denote the actual values of *C(t)*, and the solid line enotes the best fit to a biexponential decay.

Mathematical modelling in drug design

Dr. M. C. Bagchi and group

The major objective of the present project is to study some important topological and molecular complexity indices of known active compounds as well as many active analogs of the same to determine molecular similarity and performing multi parameter regression analyses for developing quantitative structure activity relationships that might help in designing newer tuberculostatic and other drugs.

The incidence of tuberculosis infections that are resistant to conventional drug therapy has risen steadily in the last decade. Several of the quinolone antibacterials have been examined as inhibitors of *M. tuberculosis* infection as well as other mycobacterial infections. However, not much has been done to examine specific structure-activity relationships of the quinolone antibacterials against mycobacteria. Most of the antimycobacterial compounds do not have sufficient physicochemical data, and thus predictive methods based on experimental data are of limited use in this situation. Hence there is a need for the development of quantitative structure-activity relationship (QSAR) models utilizing theoretical molecular descriptors that can be calculated directly from molecular structures. Descriptors associated with chemical structures of N-1 and C-7 substituted quinolone derivatives as well as 8-substituted quinolone derivatives with good antimycobacterial activities against *M. fortuitum* and *M. smegmatis* have been evaluated. Ridge regression (RR), Principal component regression (PCR), and partial least squares (PLS) regression were used, comparatively, to develop predictive models for antibacterial activity, based on the activities of the above compounds. The independent variables include topostructural, topochemical and 3-D geometrical indices, which were used in a hierarchical fashion in the model development process. The predictive ability of the models was assessed by the cross-validated R2. Comparison of the relative effectiveness of the various classes of molecular descriptors in the regression models shows that the easily calculable topological indices explain most of the variance in the data.

During the past year an attempt has also been made to formulate quantitative structure-activity relationship modelling of 2,5-Bis (1-Aziridinyl) 1,4-Benzoquinone (BABQ) compounds having activities against murine tumours from the standpoint of calculated molecular descriptors. Various molecular descriptors such as physicochemical, constitutional, geometrical, electrostatic and topological indices of such compounds have been calculated and QSAR models have been developed considering *in vitro* and *in vivo* biological activities. To establish a relationship between activity and structural descriptors of BABQ compounds, it is essential to develop a regression or an input-output model. As the number of molecular descriptors exceeds the number of observations to a large extent, conventional regression methodologies are of no use in such types of studies. Hence, QSAR models based on the large set of theoretical molecular descriptors have been developed using the ridge regression methodology that seems to be the most appropriate because of the number of independent variables greatly exceeding the number of observations and also due to the nature of the independent variables being highly inter-correlated. Finally the model was applied for prediction of a new promising, proposed to be a highly active, BABQ compound and it is seen that our model is in good agreement with the hypothesis in terms of *in vitro* and *in vivo* activities.

Elucidation of structure-function relationships of proteins and their complexes with biologically active molecules using molecular modelling techniques

Dr. C. N. Mandal and group

In continuation of our structural bioinformatics studies on sugar-binding proteins we modeled the three-dimensional structures of four newly identified putative periplasmic glucose/galactose-binding proteins (GGBP) with amino acid identities between 30 and 48% with a recently determined structure of a GGBP protein from *Salmonella typhimurium* as well as their complexes with glucose and galactose.

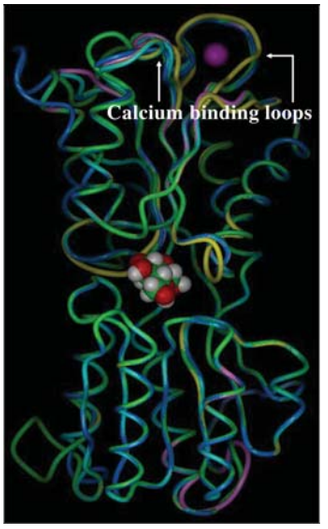


Fig. 2A: Ribbon representation of the superposed structures of the modeled proteins with the crystal structure of 3GBP. The ligand molecule is shown in space filling representation and is colored by atoms. Ribbon colors are as follows: cyan for GGBP from *Salmonella typhimurium*; light pink for model of protein from *Actinobacillus pleuropneumoniae*; light green for model of protein from *Clostridium tetani*; light blue for model of protein from *Treponema pallidum*; and light yellow for model of protein from *Pseudomonas syringae*.

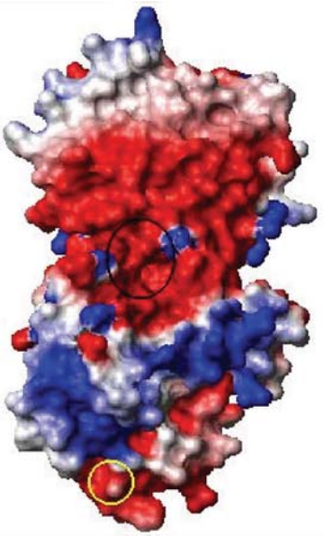


Fig. 2B: Electrostatic potential surfaces of the modeled protein a hypothetical protein of Actinobacillus pleuropneumoniae with 48% amino acid identity with 3GBP;. Blue region represents positively charged environment, red for negatively charged, and white for hydrophobic surroundings. The calcium-binding site is shown by yellow band and glucose-binding site by black band.

We could successfully identify the key residues involved in coordination with calcium ion spanning over two loop structures (2A). We calculated the ligand-binding affinities and hydrogen bonding patterns of the modeled structures and compared with those of the x-ray structure (2B). The calculation of free energies of binding of the modeled structures to glucose and galactose in the presence of water suggested that two of four putative proteins can form complexes with dissociation constants in the micromolar range (1-10 μM). Electrostatic potentials on the surfaces near the sugar and calcium-binding sites of the modeled structures were predominately negative as found in case of the x-ray structure. Taken together, our results suggest that the products of two newly discovered genes would serve as receptors for the transport of glucose and galactose.

In another project, we modeled the structures of serine proteases of four important clans e.g. PA/SA, SB, SC and SE as classified by the MEROPS database. The aim of this thesis work has been to explore the structural features of different proteases of a few clans containing serine proteases from diverse groups of the living kingdom over a wide evolutionary span ranging from bacteria to mammals (bacteria, archea, protozoa, fungi, plant and animal) with the focus on the catalytic sites and their interactions with specific inhibitors using advanced molecular modeling techniques. As this study aimed at structural studies covering 6 groups of each clan, prediction of structure was done in the cases where experimental structure was not present in the protein data bank (PDB); presence of some experimental structures of the same clan was desirable for comparing the predicted structures. Experimental structures were taken from PDB for groups for which they were available, and for the rest of the groups, one sequence each was selected for structure prediction by molecular modeling. Preference was given to homology based modeling, if known structure(s) of significant homology were present; otherwise, threading based modeling method was used. Initial models obtained from web based servers were refined with respect to backbone conformation, side chain placement, overall atom clash scores, deviations from standard bond length and angles, etc. Various structural properties of the modeled proteases were compared with the proteases of the same clan. Secondary structures and surface electrostatic potentials were calculated and compared among the members of the clan.

The knowledge of enzyme-inhibitor interactions is essential in the advanced field of rational drug design in structural bioinformatics. Therefore, a number of experimental structures of the enzyme-inhibitor complexes were analyzed to examine the nature of interaction of the enzymes with their specific inhibitors in reference to the catalytic specificity pockets. Various structural parameters like hydrogen bonds, contributions of van der Waals and electrical components to the empirical interaction energy, free energy of complex formation, and polarity of interacting atoms were calculated and compared with the experimental values. Some modeled structures of proteases were used to predict the structures of complexes with known inhibitors and their energies of interaction were compared with the structures of complexes determined by experimental methods.

The following fig. 3 shows the structures of some modelled proteases and their inhibitors:

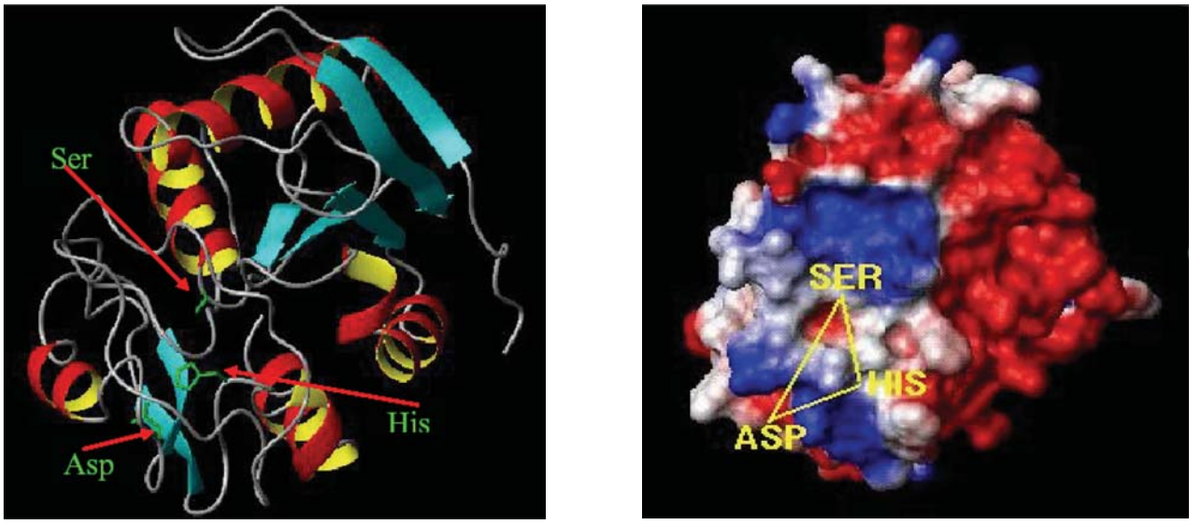
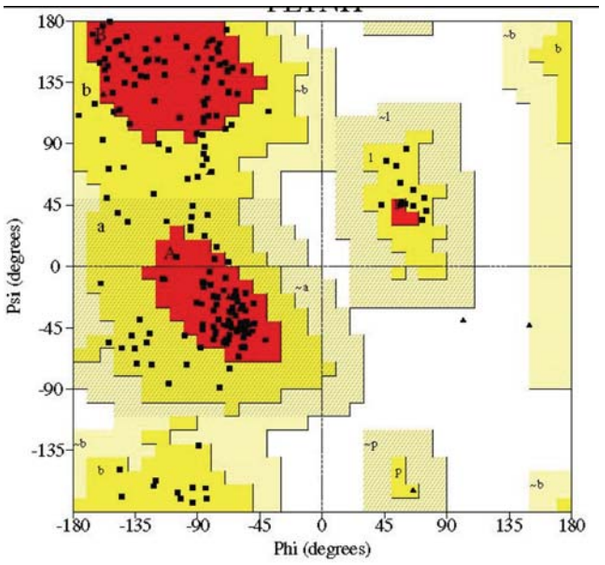
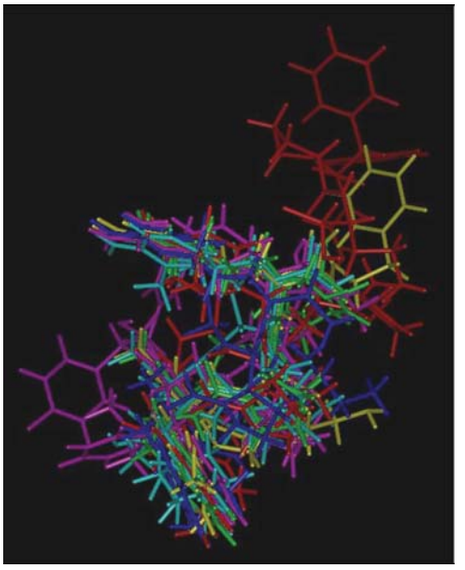


Fig. 3 : Secondary structure (left panel) and surface electrostatic potentials (right panel) of the protozoal protease from *Plasmodium falciparum* (MEROP No MER35185) of the SC clan. In secondary structures β-sheets are shown in light blue with an arrow pointing to C-terminus, (-helices are shown in red & yellow, turn/loops are shown in gray and side-chains of catalytic triad residues are shown in green sticks. In surface electrostatic potentials red, blue and white colours represent negative, positive and neutral electrostatic potentials respectively. Catalytic triad residues are shown at the corner of a triangle and both the figures are generated in the same orientation using MOLMOL.



Ramachandran's plot of the φ–ψ dihedral angles of the modeled structure of the protozoan protease from *Plasmodiun falciparum* after (left panel) refinement of the backbone conformations showing no outlier.



Structures of the inhibitors bound to the active site of thrombin obtained by superposing the structures of the complexes with respect to the common Cα-atoms of the protein.

Identification and analysis of patterns and anomalies in microbial/mammalian genome sequences

Dr. Chitra Dutta and group

Polarized trends in nucleotide and amino acid substitution patterns in human and mouse orthologs of two compositional extrema : A drive to greater divergence in human

A genome-wide analysis of sequence divergence patterns of 12198 human-mouse orthologous pairs revealed that the trends in nucleotide and amino acid substitution patterns in orthologs of high and low GC-composition are highly asymmetric and polarized to opposite directions. As the GC_3-contents of human and mouse orthologous pairs exhibit a strong positive correlation ($r= 0.86$, $p<10^{-7}$), the entire dataset was divided into three broad groups on the basis of the GC3-content of human genes: (i) High-GC ($GC_3>70\%$), (ii) Medium-GC ($70\%=GC_3=50\%$) and (iii) Low-GC ($GC3<50\%$). The analysis showed that at nucleotide level, the high-GC orthologs have undergone a large excess of AT→GC substitutions over GC→AT substitutions from mouse to human individually in all three codon positions, while for low-GC orthologs, the reverse is true. Consistent with these trends, the amino acid substitution also exhibit definite, but opposite patterns in high-GC and low-GC orthologs. High GC-orthologs exhibit significant bias in favor of Thr→Ala , Ser→Ala, Ser→Pro, Val→Ala, Lys→Arg, Asn→Ser, Ile→Val etc from mouse to human,, while in low Gc-orthologs, the reverse trends prevail. The members of the GC-even group share some trends with the high-GC group and some with the low-GC group. These observations imply that there is a definite directionality in substitution patterns towards increasing compositional divergence in human protein-coding regions as compared to mouse. Surprisingly enough, the trend Asp→Glu from mouse to human is shared by the members of all three groups of orthologs irrespective of their GC-bias, the structural/functional implication of which is not very clear.

Comparative codon and amino acid composition analysis of tritryps-conspicuous features of Leishmania major

Leishmania major, Trypanosoma brucei and Trypanosoma cruzi are the three closely related kinetoplastid parasitic protozoa, often referred together as "Tritryps". The parasites cause some of the most debilitating diseases of humankind like cutaneous leishmaniasis, African sleeping sickness, and Chagas disease, respectively. Despite the similarities in a number of biochemical and molecular characters, the pathogens differ in their life-style, propagation, pathogenesis and mode of host immune evasion. A comparative analysis of codon and amino acid usage in different groups of genes/gene-products of these three parasites revealed that gene expressivity and GC-bias play major roles in shaping gene composition of three parasites, and protein composition of *L. major* only. In *T. brucei* and *T. cruzi*, major contributions to amino acid variation come from hydropathy and/or aromaticity. Principle of Cost Minimization is followed by *T. brucei*, disregarded by *T. cruzi* and opposed by *L. major*. Slowly evolving highly expressed gene-products of *L. major* bear the signature of relatively AT-rich ancestor, while faster evolution under GC-bias have characterized the lowly expressed genes of the species by higher GC_{12} -content.

Appreciable differences in codon and amino acid usage patterns also exist among specific groups of genes/gene-products of the African and American trypanosomes i.e *T. brucei* and *T. cruzi*, respectively. Most interesting among them are the diverse trends in codon and/or amino acid usage in the immunogenic arsenals of the two trypanosomes, i.e., the variable surface glycoproteins (VSGs) of *T. brucei* and mucin-like proteins (MUCINs) of *T. cruzi*. Among the other fascinating observations made in the present study are the significant contributions of cell surface proteins with cysteine-rich repeat motifs (CSPs) and potential horizontally transferred genes to intra-genomic variations in codon/amino acid usages in *T. cruzi*. VSGs of *T. brucei* are marked by high values of C_3+A_3, low potential expressivity and overrepresentation of Ala, Thr, Gln, Asn, Lys etc. In *T. cruzi*, MUCINs are characterized by low aromaticity and high alcoholicity; some potential horizontally transferred genes are distinguished by A+T-rich codon usage and CSPs are typified by high potential expressivity, abundance in

hydrophobic residues, paucity of charged residues and presence of potential transmembrane domains and ordered globular structure.

Analysis of gene and protein architectures of extremely halophilic microorganisms - molecular signature of hypersaline adaptation

A large scale comparative study of the compositional characteristics of genomes and proteomes of the extreme halophilic and non-halophilic microorganisms has revealed the conspicuous characteristics relevant to life in an extreme environment distinguished by hypersalinity. These are

(i) distinct synonymous codon usage,

(ii) enhanced usage of negatively charged residues on protein surface,

(iii) decreased frequencies of hydrophobic residues, and

(iv) higher propensities for formation of random coil region in proteins, as compared to their orthologs in non-halophilic organisms.

Comparison of 124 orthologous protein sequences from halophilic and non-halophilic species of comparable genomic G+C contents has shown a strong bias towards replacement of positively charged and hydrophobic residues of non-halophilic proteins by Asp and Glu in halophiles. Higher propensity of formation of random coil region and surface negative charge distribution are evident from the previously reported experimentally determined three dimensional orthologous structures of halophiles and non-halophiles (Fig. 4).

The analysis not only demonstrates that genes/proteins of the extreme halophilic organisms are magnificently engineered in order to survive in the high salt condition, but also offers an insight into the nitty-gritty of the molecular strategies adopted by the microbial world to optimize between their functional activities and structural stability in such a specialized niche.

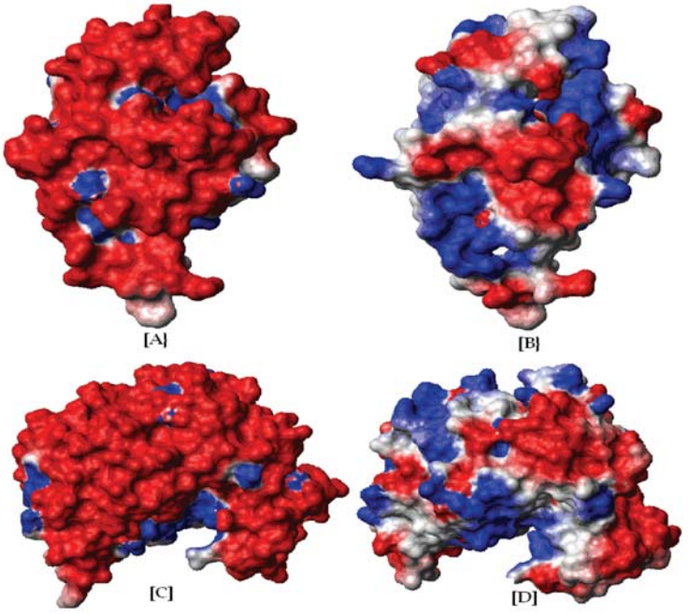


Fig. 4: Surface charge distributions for the Elongation factor Tu (EF- Tu) proteins *E. coli* [A] and *N. equitans* [B] and the Cell division cycle family protein from *M. maripaludis* [C] and *N. equitans* [D]. Basic regions are indicated by blue, acidic regions are indicated by red and neutral region is indicated by white.

Functional regulation and assembly of multimeric enzymes, stability and spectroscopic properties of enzymes, characterization of venom toxins and the drug 'Placentrex'

Dr Debasish Bhattacharyya and group

Functional regulation of epimerase: The NAD bound dimeric enzyme, UDP-galactose 4-epimerase plays a central role in galactose metabolism while converting UDP-galactose to UDP-glucose. Allosteric regulation of this enzyme from *Klyuveromyces fragilis* has been studied. At present it has been conclusively proved that each subunit of the enzyme is functional. The enzyme has distinct high and low affinity sites for substrate and inhibitor. Under controlled conditions of 'reductive inhibition', one of the catalytic sites could be inactivated whereby the biphasic Michelis-Menten relation is reduced to monophasic dependency. The enzyme also behaves differently with the substrates UDP-gal and UDP-glu in terms of inactivation related to catalytic turnover. It appears that the transition state of the reaction converting UDP-galactose is unstable and the intermediate complex is dissociated after chemical reduction as a result the enzyme is irreversibly inactivated. This is also a mechanism by which the activity of the enzyme is controlled.

The origin of stability of proteins is an important and complicated issue that is poorly understood. Many proteins through evolutionary processes adapt a mechanism called 'kinetic stability' where the energy of activation between the native and denatured state remains very high so that their inter-conversion is not permitted. Bromelain - a cysteine protease from pineapple stabilizes from this mechanism. General structural and chemical features of proteins required for kinetic stability have been fulfilled for bromelain. These are β-sheet rich structure, resistance to proteolysis and SDS binding and of course high E_{act} of inactivation and unfolding. The results justify application of bromelain in industrial uses where stability of a protein/enzyme is a matter of concern.

Significant advances have been made in venom research. A low Mw protein of 7-kDa has been isolated from the venom of Russell's viper. It possesses several toxicological properties like PLA2 activity, cytotoxicity, trypsin inhibitory property, tumor growth inhibition and also strong damaging activity towards mice kidney. Since acute renal failure is a common feature of RVV envenomation, further studies indicated that it was the major component of the venom, which is responsible for renal failure in experimental animals. Its basic character and small size are favorable features for attraction of kidney membranes and infiltration into the organ.

Characterization of the drug 'Placentrex', an aqueous extract of human placenta used as efficient wound healer, in terms of chemical composition and mechanism of action is a continued effort from 1999. Recently, we have confirmed using FRET analysis that the fibronectin type IIIC like peptide present in the extract can act as trypsin inhibitor. Earlier stabilization of trypsin activity in presence of the peptide was demonstrated. The affinity between the enzyme and the peptide being very strong (comparable to soyabean trypsin inhibitor), it remains elusive at present how trypsin get released *in vitro* (or *in vivo*) in presence of its substrates.

In-silico studies for rational drug design and receptor modelling

Dr. Nanda Ghoshal and group

Exploration of rate-limiting conformational state for 5-[(7-Chloro-4-quinolinyl)amino]-3-[(alkylamino)methyl][1,1' biphenyl]-2-ols and N^-Oxides (Tebuquine analogues) for antimalarial activity using molecular shape analysis and molecular field analysis studies

Tebuquine is a 4-aminoquinoline that shows significantly more potency as an antimalarial than amodiaquine and chloroquine both *in vitro* and *in vivo*. To explore the conformation in the rate-limiting step and to elucidate pharmacophoric properties of tebuquine-related analogues, molecular shape analysis (MSA) along with molecular

field analysis (MFA) methods were applied on a series of 5-[(7-chloro-4-quinolinyl)amino]-3-[(alkylamino)methyl][1,1'-biphenyl]-2-ol analogues and their Nˆ-oxides (Fig. 5) possessing antimalarial activity. Both methods were analyzed in terms of their predictive abilities and produced comparable results with good conventional and cross-validated *r*2 values (0.908 and 0.886, respectively, for the MFA model and 0.846 and 0.812, respectively, for the MSA model). In external data set prediction, the MSA model (Fig. 6) scored much better than MFA. Steric, electrostatic, and hydrogen-bond donor/acceptor fields of molecules were found to be relevant descriptors for structure-activity relationships. The inclusion of polar solvent-accessible charged surface area and spatial descriptors in the MSA model generation resulted in a model with significant predictive ability for the test set molecules. This indicates the importance of the orientation of conformationally favored molecules inside the receptor site and solvation of the charged surfaces of the molecule by a polar solvent for the activity of the molecule. The results provided the appropriate tools for predicting the affinity of related compounds using a ligand based approach, and for guiding the design and synthesis of novel and more potent antimalarial agents.

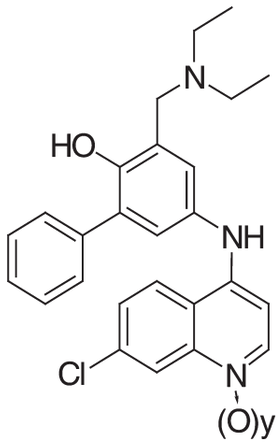


Fig. 5: Structure of 5-[(7-chloro-4-quinolinyl) amino] and 3- [(alkylamino) methyl][1,1'-biphenyl]-2-ol Y =0, des-N-oxide; Y =1, N-oxide

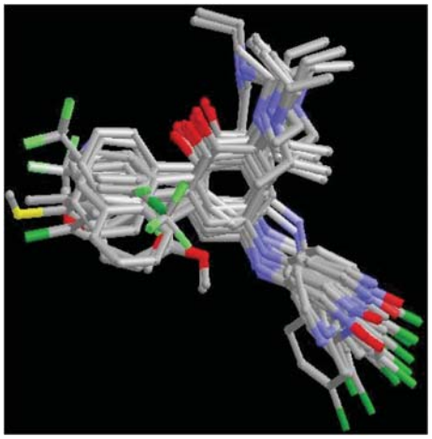


Fig. 6: Superimposition of training set molecules using 'MCSG' method in most probable bioactive orientations obtained by best MSA QSAR model. The atoms of molecules are depicted as cylinder models with no hydrogen shown.

Structure based pharmacophore generation and 3D QSAR analyses of benzothiazol-2-yl- acetonitrile pyrimidne core based derivatives as potent C-JUN N-terminal kinase-3 inhibitors

C-Jun N-terminal kinase (JNK) is a therapeutic target for inhibitors which may provide clinical benefit in the pathogenesis of rheumatoid arthritis (RA), as well as in various apoptosis-related disorders. The benzothiazol-2-yl acetonitrile derivatives are the first generation JNK inhibitors of this class. To understand inhibitory mechanism and elucidate pharmacophoric properties of these derivatives molecular docking and 3D-QSAR studies were performed on a set of 44 compounds. Based on the binding conformations, robust and highly predictive 3D-QSAR models were developed (N. Ghoshal et al., *Journal of chemical information and modeling,* 46, 1763-1774, 2006).

The interaction mode was demonstrated taking into consideration inhibitor conformation, hydrogen bonding and electrostatic interaction. The information, obtained about binding mode and conformations was used to generate structure based pharmacophores. Five different optimized pharmacophores were generated. Best hypothesis contains two HBA (hydrogen bond acceptor), one HBD (hydrogen based donor), one Hydrophobic

and two Aromatic Ring features along with docked shape of the most active inhibitor. These features were found in accordance with the key interacting residues. The Structure based pharmacophore model generated in this study provided clear guidelines for novel inhibitor design as well as for virtual screening to find new leads against JNK-3 for the treatment of inflammatory disorders (Fig. 7A & 7B).

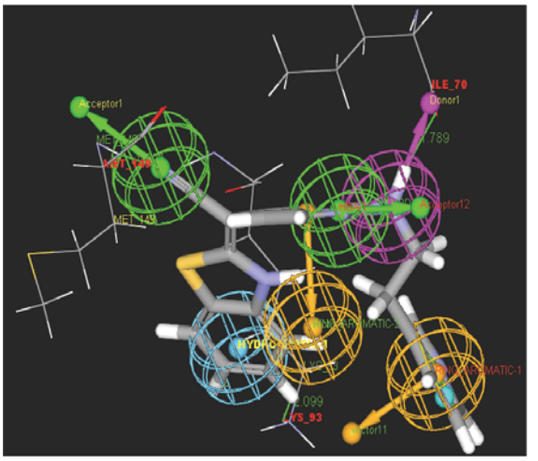


Fig. 7A: based on the ligand-receptor complex. Only key interaction- residues are shown for clarity.

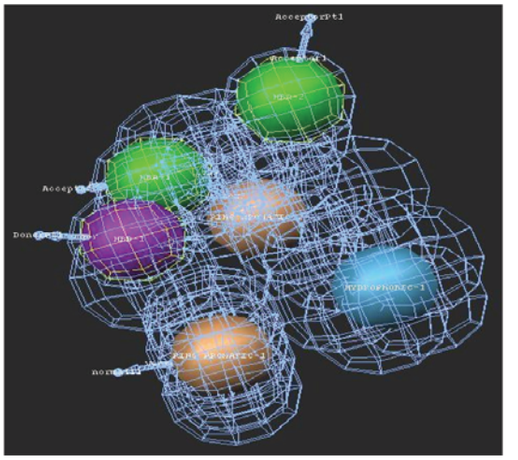


Fig. 7B: Merged hypothesis based on shape & features constraint of most active JNK3 inhibitor in docked conformation

QSAR study on aminoquinonoid analogues of diospyrin for antitumour activity

A QSAR study was performed, using genetic function approximation, on a dataset of diospyrin and its amino derivatives (obtained from Department of Pharmaceutical Technology, Jadavpur University under collaborative work). The best QSAR model with generalized r2 = 0.999 and full cross-validation r2 = 0.984 could provide clear guidelines for designing novel antitumour agents based on amino-diospyrin template (Fig. 8).

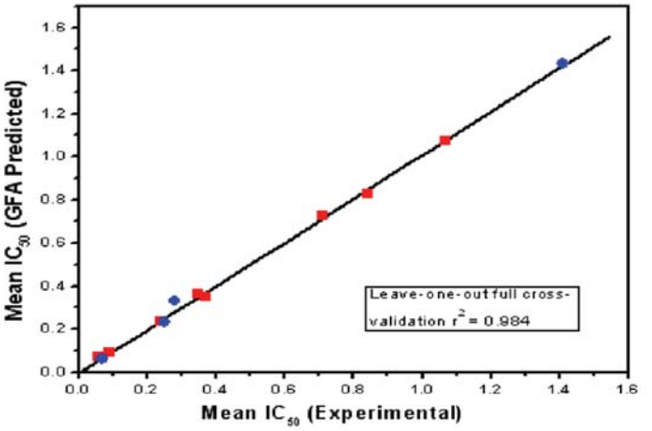


Fig. 8: The scatter plot of experimental versus predicted antitumour activity of diospyrin derivatives against EAC *in vitro*, based on GFA model ; ¦ training compound; • test compound.

Preliminary QSAR studies showed that fragment-based sterimol parameters and spatial arrangements of substituents, charged partial surface area, HOMO energy and molecular shape Kappa indices of this class of compounds would play significant roles in eliciting their antitumour property. Evidently, the above findings would lead to the development of more effective analogues through judicious modification of the diospyrin template. On the basis of information obtained from this model, several new structures were designed hypothetically. Two such molecules could be synthesized followed by determination of the cytotoxicity in EAC cells in vitro (by the collaborating group in Department of Pharmaceutical Technology, Jadavpur University). Significantly, the 'observed' IC50 were found to be very close to the 'predicted' values). This indicated the statistical reliability of the model, despite the relatively small number of candidates, for predicting high efficacy ligands to design prospective amino-analogues of diospyrin with improved antitumour activity.

A computational docking study for prediction of binding mode of diospyrin and derivatives: Inhibitors of human and leishmanial DNA topoisomerase-I

A computational approach was utilized to study the relative binding modes of diospyrin (bisnaphthoquinonoid) with the crystal structure of human DNA-TopoI and the recently reported *Leishmania donavani* DNA-TopoI. Additionally, the binding site interactions of amino derivatives of diospyrin with human TopoI were studied extensively. Based on the docking results, binding modes of diospyrin with the human and leishmanial TopoI catalytic core were predicted. The parallel use of two efficient and predictive docking programs, GOLD and Ligandfit, allowed mutual validation of the predicted binding poses. A reasonably good correlation coefficient between the calculated docking scores and the experimentally determined cytotoxicity (data mentioned under point C) helped in validating the docking method. Furthermore, a structure-based pharmacophore model was developed for L. donavani DNA-TopoI inhibition which helped in elucidating the topological and spatial requirements of the ligand-receptor interactions. This study provides an understanding of the structural basis of ligand binding to the topoisomerase receptor, which may be used for the structure-based design of potent and novel ligands for anticancer and antileishmanial therapy. To our knowledge, this is the first report of a binding mode exploration study for diospyrin and its derivatives as inhibitors of the leishmanial and human TopoI enzymes.

Contribution in BlockII units for Mtb database

Contributed by giving inputs for modification of input fields in the data base structure for unit 2.5 (second line drugs - structure activity) and unit 2.6 (drug failures) for Mtb database.

3-Dimentional structural investigations of biological macromolecules

Dr. Saumen Datta & group

Structural investigation of some virulent proteins from Pseudomonas aeruginosa

Pseudomonas aeruginosa is a gram - negative, aerobic, rod shaped bacterium with unipolar motility. It is an opportunistic pathogen of immunocompromised individuals, typically infecting the pulmonary tract, urinary tract, burns, and wounds and also causes other blood infections. *P. aeruginosa* for its pathogenic activity uses a type III secretion system to inject toxic effector/virulent proteins into the cytoplasm of the eukarotic host cells. From genomic analysis four effector (virulent) proteins so far have been identified in *P.aeruginosa*: exoS, exoT, exoU and exoY. We are in the process of cloning and expressing the above mentioned virulent proteins in recombinant manner to do the crystallization studies of these proteins. The diagram below (Fig. 2) shows the PCR products of the virulent proteins from the genomic DNA of *P.areuginosa* strain 2192 (ATCC 39324).

Complete genome sequence of *Pseudomonas aeruginosa* is mainly available for three strains mainly PA01, PA7 and PA14. *P.areuginosa* 2192 (ATCC 39324) is an incomplete sequenced strain seemed to be derived from PA01 strain. We were able to get the PCR products of the genes correspond to the proteins exoS, exoT, and exoY (as shown in Fig. 9). Since our strain 2192 is derivative of PA01 in which exoU is absent so we could not obtain the PCR product of the respective gene.

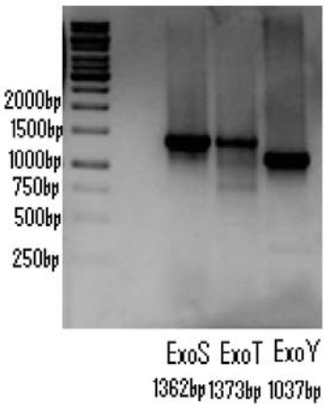


Fig. 9: Lane 1 shows the DNA ladder as marked by the corresponding base pairs (bp) at the left side. Lane 2 is blank. Lane 3, 4 and 5 show the PCR products from *P. areuginosa 2192* (ATCC 39324) genomic DNA for the virulent proteins ExoS, ExoT and ExoY respectively and are indicated under each lane. The size of the respective genes marked in bp is also given below the respective lanes.

X-ray crystallographic characterization some of the spindle assembly checkpoint proteins and their complexes.

The spindle assembly checkpoint is one of the surveillance mechanisms to protect cells from genomic instability and it prevents mis-segregation of chromosomes .The spindle assembly checkpoint is controlled by the Bub-Mad pathway. This pathway involves Mad1, Mad2, Mad3, Bub1, Bub3, BubR1, CDC20 and Mps1 gene products of which Mad2- CDC20 interaction plays an important role.
As we are trying to study the interaction between the two proteins Mad2 and CDC20, it will be highly important to get the co-crystal structure of these two. In this connection the experiments already performed and the future directions are described below:

1) C terminal His tagged Mad2 was purified with Ni-NTA column.

2) Since the C terminal of CDC20 is well structured but the N terminal is flexible, it is difficult to express full length CDC20. So we are working with two fragments of it: a) One deletion construct of CDC20 named GM3, where the N terminal is absent and b) a short C terminal peptide of CDC20. This peptide has already been synthesized and biochemical characterization of the interaction is under way.

To check the interaction between these two proteins (Mad2 and GM3) at present we are trying to reclone GM3 in a GST tagged vector, pGEX-5X-2 from pGEP vector (Fig. 10). We are also trying to find other proteins that might interact with CDC20 (Gm3). This could be achieved by binding Gm3 in GST column and passing crude cell extract over it.

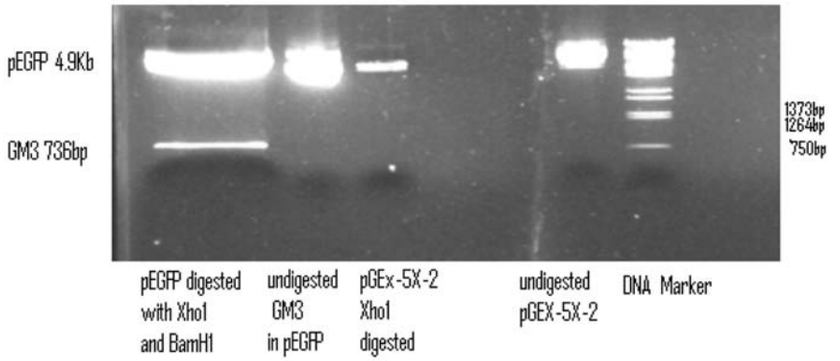


Fig. 10: Lane 1 shows the digested product of pGEP vector with GM3. The vector was digested by Xho1 and BamH1. The two bands, top one the linear pGEP vector without GM3 (4.9 Kbp) and the second one correspond to GM3 (736bp). Lane 3 shows the linear pGEx-5X-2 digested by Xho1. Other lanes' bands are also marked at the bottom of the respective lanes. The last lane shows the DNA marker.

Protein folding and fluorescence correlation spectroscopy

Dr Krishnananda Chattopadhyay and group

We are studying protein folding using a large number of biophysical and biochemical techniques with particular emphasis to Fluorescence correlation spectroscopy (FCS). FCS is an important technique in biochemical studies to study diffusion as well as conformational transitions on time scales of (sec and longer. It involves measuring fluorescence fluctuations under conditions of thermodynamic equilibrium in a small observation volume. These fluctuations may result either from a change in the number of fluorophores in the observation volume due to diffusion or a change in fluorescence properties of the molecule as a consequence of a chemical reaction or a conformational fluctuation (Chattopadhyay, K. et al. (2005) Biophysical Journal **88**, 1413-1422). We have recently reported the first application of FCS to protein folding and measured (sec conformational dynamics of intestinal fatty acid binding protein (IFABP) in its native and unfolded states (Chattopadhyay, K. et al. (2005) Proc. Natl. Acad. Sci (USA) **102**, 2385-2389; Chattopadhyay, K. et al. (2002) Proc. Natl. Acad. Sci. (USA), **99**, 14171-14176).

We have recently setup a new laboratory at IICB to carry out FCS experiments to understand the mechanistics and dynamics of protein folding problems. The Confocor III setup from Carl Zeiss has been successfully installed and has been fully operational. The following is a picture of a typical correlation function observed in our setup using tetramethyl rhodamine at pH 7.4. The data was fit (the red line shows the fit) to a model of a single diffusing species with the diffusion time of 33 sec. A number of proteins have also been labeled with different dyes and their correlation functions have been observed successfully with the new system. We are also in the process of establishing a new laboratory for the regular experiments like molecular biology, expression and purification of proteins, labeling proteins with synthetic conjugates and other biophysical characterizations.

Biochemistry of a novel plant like ascorbate peroxidase from Leishmania major

Dr. Subrata Adak and group

Intracellular microbes like Leishmania residing in the macrophages of mammalian hosts must rise to the deadly oxidative challenge by preventing oxidant formation, resisting the damage from toxic oxygen products, or metabolizing the oxidants. Hence the Leishmania species have developed a diverse array of mechanisms allowing

them to scavenge toxic oxygen products and inhibit macrophage responses. Though previous studies have shown that heme peroxidases and catalase play a major role in H2O2-detoxification in most aerobic organisms, but Leishmania species have so far been reported to lack this activity. Recently, by using classical molecular biology techniques we have cloned and expressed the *Leishmania major* ascorbate peroxidase (LmAPX) enzyme as a N-terminal His-tag protein. This is the first unusual plant-like heme peroxidase discovered from Leishmania species. Examination of the nucleotide-derived protein sequence indicated that LmAPX is related to the class I group of hemeperoxidase having 30-35% identity to plant ascorbate peroxidases (APX). Our preliminary results indicate that the LmAPX has several features that are clearly unique with respect to other APXs e.g. (a) in contrast to cytosolic APXs, LmAPX contains an amino terminal extension of 34 residues which is distinct in that it contains leader sequence followed by a stretch of 22 hydrophobic amino acids having potential to form a transmembrane domain, (b) The specific activity of ascorbate and guaiacol oxidation by LmAPX is lower compared to the plant APX and most interestingly (c) in spite of being capable of oxidizing ascorbate, the crucial ascorbate binding residue, corresponding to that of plant APXs, is absent in this enzyme suggesting different binding mechanism. Despite these very little is known about the biochemical features of this parasitic enzyme that includes the active site residues controlling heme activation, ligand binding, substrate specificity and electron transfer pathways. Detail investigation is also required to understand the precise intra-cellular localization, its physiological function and regulation of LmAPX within the cell. With this background information we have taken a two-pronged approach to study the biochemistry of LmAPX with an objective to address the following fundamental questions: (a) How the Leishmania peroxidase is different from other well-known peroxidases with regard to its catalytic properties. (b) What is/are the exact physiological function(s) of LmAPX, where this enzyme is localized within the cell and how the expression of the enzyme is regulated in different life-cycle stages of the parasite.

Technical Officers

Mr. Samir K. Roy, Mr. Prosenjit Gangopadhyay, Mrs. Aparna Laskar, Dr. Subhagata Ghosh

Technical Assistant

Mr. Jishu Mandal

Pool Officers, RAs, Research Fellows

Dr. Indrani Chowdhuri; Dr. Ruchira Mukherjee; Dr. Sampa Mallick; Dr. Atanu Chatterjee; Paromita Raha; Asit Kr. Manna; Subrata Debnath; Neeladri Sekhar Roy, Avishek Majumder, Prasenjit Chakraborty, Sisir Nandi, Payel Ghosh, Sujata Majumdar, Madhumita Patra, Anirban Datta, Munmun Sarkar, Gargi Maiti, Sangeeta Nath, Reema Bhattacharya, Somnath Mondal, Debashree De, Nupur Sengupta, Debratna Saha, Srinjana Ghosh, Savita Bhutoria, Nahren Manuel, Pooja Sharma, Sandeep Chabra, R.Vijayan, Sunny Sharma, Ranendu Ghosh, Supratim Dey, Anindya Roy Chowdhury, Subhankar Dolai; Rajesh Yadav; Swati Pal

Summer Trainees

Sirshendu Chatterjee, Debratna Saha, Divya Rose T. G., M. Prabu

Mission Mode Projects

There are three categories under the Mission Mode Projects : Core programmes identified by CSIR TFYP Working Group, *i.e.*, COR; Mission mode programmes identified by the Screening Committee, *i.e.*, SMM; Mission mode programmes identified by CSIR TFYP Working Group, *i.e.*, CMM. IICB coordinated one Mission Mode Project and participated in 13 Mission Mode Projects as participating laboratory.

IICB AS THE COORDINATING LABORATORY

1. Asthmatic and Allergic Disorders Mitigation Mission (SMM 0006)

Objectives as stated in the project proposal:

I. Targets & Leads : identification and optimisation

It is known that asthma is manifested via the mediation of 5-LO, (a leukotriene producing enzyme), 5-LO activating protein (FLAP), Th2-cytokines like IL4, IL5, IL13, IgE and phosphodiesterase (PDE), etc. Therefore, it would be of prime importance to target these molecules for mitigating asthmatic and allergic disorders.

[a] Immediate targets, such as IL4, IL5, IL13 having Th2 response will be attempted to reverse towards Th1 response, i.e., increase of IFN-γ, etc. with natural sources & other compounds including synthetically promising molecules.

[b] Late phase targets would be 5-LO, FLAP, IgE, PDEs, Phospholipase (PLA2), leukotrienes, lund surfactant proteins (SP)-A & -D (SPA & SPD).

[c] Extraction, identification, purification of herbal preparations/molecules, showing activity on early & late phase pathways mentioned in a & b.

[d] Chemical screening by finger printing and purification by gel-permeation, ion-exchange & reverse phase chromatography.

[e] Screening of promising molecules through *in vivo* animal models.

[f] Determination of chemical structure of effective molecules, designing of the molecules for better performance & chemical synthesis.

[g] Identification of new pollens and fungal allergens for creating awareness among the masses.

II. Genetics & Predictive Medicine

[a] Determination of the genetic basis of asthma, study of genetic interactions between causative agents and concerned genes with a view to adopting predictive measures.

[b] Development of predictive medicines related to asthmatic and allergic disorders using repeat and SNPs based on the studies of population genetics and genomic data.

III. Toxicological/Safety Evaluation

Once excitingly promising preparations/molecules or active principles are obtained, determination of toxicity in terms of acute and chronic effects in animal models will be taken up. Safety evaluation of newer molecules will be carried out as per OECD guidelines.

IV. Pharmacology

Pharmacokinetics of the available active preparations/molecules to determine precise dosage, bioavailability, retention time *(in vivo)* etc. will be studied to cover the regulatory requirements for a drug preparation.

V. Mechanisms of Action

Finally emphasis will be given to explore the mechanism of actions of the preparation/molecules on specific target sites to strengthen the claim with a view to mitigating asthmatic and allergic disorders. Biochemical, immunological, genetically and pharmacological aspects will be covered.

Detailed analysis of results indicating contributions made towards fulfilling identified gaps in knowledge and/or technology

Activity-guided fractionation of two hundred plant extracts were performed for identification of lead molecules against important targets involved in bronchial asthma namely 5-Lipoxygenase (5-LO), cytosolic phospholipase A2 (cPLA2), phosphodiesterase E4 (PDE4). Activity-guided fractionation was also performed for inhibition of pro-inflammatory cytokines. One hundred and seventy nine molecules were synthesized around rolipram backbone, a known inhibitor of PDE4 but has adverse toxicities. The idea was to synthesize non-toxic inhibitors of PDE4. These molecules have been screened for inhibition of PDE4.

Activity-guided fractionation led to purification of four lead molecules from plants for inhibition of c-PLA2, PDE4 and pro-inflammatory cytokines namely TNF-α, IL-6, IL-1β, IL-8. One molecule (ICB14-C6) inhibited these pro-inflammatory cytokines. Two other molecules (ICB11-D6, ICB11-D8) inhibited PDE4. Another molecule (ICB11-D10) inhibited c-LPA2. Eight synthetic molecules (ICT52, ICT55, ICT57, ICT67, ICT83, ICT97, ICT100, ICT102) also inhibited PDE4. A total of 119 synthetic molecules have been tested for inhibition of tumor necrosis factor-alpha (TNF-α) and bacterial lipopolysaccharide (LPS)-induced expression of intercellular adhesion molecule-1 (ICAM-1) on human endothelial cells. Expression of ICAM-1 is known to play an important role in bronchial asthma. Twenty eight synthetic molecules were found to induce inhibition of ICAM-1 by more than 75%.

A total of 8 compounds were tested for anti-asthmatic activity using mouse model of bronchial asthma. Two compounds, ICB14-C6 and ICT-67 were found to be effective in alleviating asthma conditions, *viz.*, decreased airway hyper-responsiveness, Th2 cytokines and lung eosinophil counts. ICB11-D6 showed partial anti-asthmatic activity *in vivo* in mouse model of bronchial asthma.

Intranasal administration of recombinant lung surfactant protein-D (rhSP-D) has been found to have a protective effect in a murine model of pulmonary hypersensitivity to DERP allergens. Apart from being therapeutically effective in the modulation of allergic sensitization, rhSP-D was found to efficiently correct the Th1-Th2 imbalance, peripheral and pulmonary eosinophilia.

Cytochrome c was established to be a major cross-reactive allergen in fungi and grass pollen. Both recombinant and native Cytochrome c showed comparable immunoreactivity by ELISA, ELISA inhibition, PBMC proliferation, Histamine release, cytokine analysis in 20 fungal positive patient sera/blood. Out of the 6 B cell & 4 T cell

peptides selected from cytochrome C, P6 was found to have high B and T cell activity. Thus, P6 could be used for the synthesis of hypo-allergenic variants.

After evaluating *in vitro* cytotoxicity studies using 3T3 cells, oral toxicity studies (both acute [14d] and subchronic [90d]) were performed in mice with the lead molecules. LD50 for ICB14-C6 is 168.345 mg/kg body weight. ICB14-C6 was further subjected to 90d sub chronic oral toxicity studies. Based on body weight, organ weight, gross necropsy, immunotoxicity, hematology, clinical chemistry and cage side observation in mice, no-observed-adverse-effect-level (NOAEL) was found to be 21 mg/kg body weight. Acute and chronic toxicity studies indicate that the molecule ICB14-C6 has wide therapeutic window: Therapeutic efficacy: 2.5 mg/kg body weight (upper limit).

The synthetic anti-asthmatic molecule ICT-67 appears safe even at a dose of 2000 mg/kg body weight. No changes in the body weight, absolute and relative organ weight, clinical biochemistry, hematology and gross necropsy were observed. Cage side observations showed no sign of behavioral changes. No mortality or morbidity was observed. As per the guidelines of Organization of Economic Co-operation Development (OECD), ICT-67 was found to be "Non-Toxic".

Detail pharmacokinetic studies were performed on the synthetic molecules ICT-45, ICT-57, ICT-62, ICT-67. These studies indicate that ICT-67 has acceptable bio-availability and phamacokinetic profile.

Four different species of mustard, studied for their allergenicity, have revealed that pollen of *Brassica campestris* are the highest sensitizers in general atopic population in India. On the contrary, seeds of *B. juncea* show high sensitivity (9.4 %) as compared to *B. campestris* (6.9 %).

Genetic variants (including few novel variants) of IL-4, IL-RA, STAT6, FcER1B, CD14, CC16, TGF-β1, IL-10, IL12B, CCR5, NAT2, iNOS, Eotaxin, TNF-α and LELP1 genes were identified and were analyzed for their association with asthma using North Indian and South Indian population. Of interest, unlike in North Indian population, polymorphisms in the IL10 gene neither at genotypic nor at haplotype level play important role for susceptibility to asthma in South Indian population. Microarray analysis using eosinophils of asthma patients and controls identified 31 up regulated and 21 down regulated genes. In particular, the polymorphisms and haplotypes in the TGF-β1, FcER1B, Eotaxin and iNOS genes were correlated with the expression profiles of their protein levels in the serum and the protective haplotypes were found to be associated with lower levels as compared to the risk haplotypes.

Salient achievements summarizing contributions made towards knowledge generation and/or technology development and research outputs

- 200 plant extracts have been screened for identification of lead molecules.
- 60 synthetic molecules have also been screened.
- 12 lead molecules have been purified or synthesized.
- One natural molecule (ICB11-D10) inhibited c-PLA2.
- Ten molecules 'two natural and eight synthetic' (ICB11-D6, ICB11-D8, ICT52, ICT55, ICT57, ICT67, ICT83, ICT97, ICT100, ICT102) inhibited Phosphodiesterase 4.
- One molecule (ICB14-C6) inhibited inflammatory cytokines.
- A total of 119 IICT compounds have been tested for ICAM-1 inhibition activity out of which 28 were found to have more than 75% ICAM-1 inhibition.
- A total of 8 compounds were tested for anti - asthmatic activity using mouse model of asthma.

- ICB14-C6 and ICT-67 showed promising activities while ICB11-D6 showed partial anti -asthmatic activity *in vivo*.
- Toxicity studies on ICB14-C6 indicate that this molecule has wide therapeutic window.
- Therapeutic efficacy : 2.5mg/kg body weight (upper limit); LD50 : 168.345 mg/kg body weight.
- Toxicity studies on ICT-67 indicate that this molecule is non toxic.
- Pharmacokinetic studies indicate that ICT-67 is orally bioavailable and has acceptable pharmacokinetic profile.
- Genetic variants of number of genes were identified and were analyzed for their association with asthma using North Indian and South Indian population with family based approaches.
- A significant association of IL-4, IL-4RA, STAT6, FcER1B, CD14, CC16, TGF-B1, IL-10, IL-12B, CCR5, NAT2, iNOS, Eotaxin and LELP1 gene variants was identified with asthma or associated phenotypes.
- Polymorphisms in IL4, IL10, IL9 and IL13 and ADRB2 are not associated with bronchial asthma in South Indian population.
- There exist important North-South differences in genetic susceptibility to bronchial asthma.

Scientific & Technical Achievements made :

- Papers in SCI Journals (Nos.) - 41
- Patents (Indian & Foreign) (Nos.) - 4
- Technology/Process/Product developed - Two anti-asthmatic lead molecules have been identified.
- Training if any imparted (Nos.) - Sixtyone (61) manpowers were trained in biomedical research (including postgraduate students, M.Sc. dissertation training).
- No. of Ph.Ds. produced - 12

IICB AS PARTICIPATING LABORATORY

1. Development of Medicinal Plant Chemotypes for Enhanced Marker and Value Added Compounds (COR 0002)

Task assigned to the laboratory:

- The task assaigned to Indian Institute of Chemical Biology, Kolkata is to isolate marker compounds from ten selected medicinal herbs namely *Andrographis paniculata, Artemisia annua, Acorus calamus, Bacopa monnieri, Catharanthus roseus, Chlorophytum borivilianum, Commiphora wightii, Picrorohiza kurroa, Podophyllum hexandrum and Swertia chirata* with an overall attempt to enhance the production of twenty two commercially important high value drug molecules present in them

Deliverables/outcome at the completion of the project from the tasks assigned to labouratory :

- Deliverables in the form of harmonized SOPs for quality assessment of the ten targeted herbs, availability of several marker compounds in pure form, value addition of known marker compounds and identification of novel marker molecules or their derivatives for new activities are some of the successes of this network project

Scientific & Technical Achievements made :

- Number of new bioactive molecules have been isolated and their stuctures have been established by detailed spectral and chemical analysis

2. Natural, Nature Identical or Nature Similar Biomolecules (COR 0010)

Task assigned to the laboratory :

- Development of methodology for isolation of saponins with high yield, Ac-A & B.
- Confirmation of spermicidal effects of the saponins
- Mode of spermicidal action of the saponins.
- Toxicity study with the effective saponin.

Deliverables/outcome at the completion of the project from the task assigned to the laboratory :

- Successful completion of the project would lead to isolation and identification of saponin(s) having spermicidal potential to be used in prospective vaginal contraceptive formulations.

Scientific and Technical Achievements made :

- Ac-B, a triterpenoid glycoside, and an Ac-B-enriched fraction extracted from the seeds of *Acacia auriculiformis* have been identified as prospective spermicidal principles.
- Both possess strong spermicidal property.
- The mechanism of action involves disintegration of the lipid layer of the sperm membrane.
- Both are effective at concentrations significantly lower than that of any marketed product including N-9.
- Ac-B prevents the growth of *E. coli* but unlike the marketed spermicides does not interfere with growth of *Lactobacillus* in laboratory culture.
- The Ames test proves Ac-B to be non-mutagenic.
- The preliminary investigation promises Ac-B to have anti-HIV property *(Currently under evaluation at National Centre for Cell Science, Pune)*.
- The preliminary toxicity study conducted so far revealed that it causes irritancy of rabbit eyes, however, the effect is transitional and has no deleterious consequences following repeated application.
- All these qualities in Ac-B highlight its potential as a future spermicidal agent.

3. Infectious Diseases: Storage, Handling and Research Facilities (COR 0011)

Task assigned to the laboratory :

- The major objective of the project is to set up a research facility as well as detection and storage of selected number of highly infected pathogens of national importance. The selected pathogens are Japanese encephalitis virus, dengue virus under the virology program and *Shigella spp*. under the bacterial infectious diseases program.

Deliverables/outcome at the completion of the project from the task/s assigned to laboratory :

- Basic research on the highly infective pathogens may help in developing effective therapeutic intervention. The proposed research work on BSL-3 grade organisms will provide rapid diagnostic information related to public health. The center will serve as a reference lab for the pathogens on which research will be conducted.

Scientific & Technical Achievements made :

- Under the tenth five year plan, CSIR has created five BSL-3 laboratories throughout the country for safe handling, storage and research on highly infectious diseases and it is expected that this type of facility need constant support for future maintenance. At IICB one such facility has been developed and which will be fully utilized for both basic and applied research on selected pathogens. Moreover, networking among the BSL-3 facilities developed at various CSIR laboratories is highly desirable for providing service under any epidemic condition and biosecurity.

4. Biomineral Processing for Extraction of Metal Values from Ores and Concentrates (COR 0020)

Task assigned to the laboratory:

- Isolation of microorganisms from mine sites
- Characterization of the above native microorganisms,
- Culture and strain- improvements towards bio-leaching .

Deliverables/outcome at the completion of the project from the task/s assigned to laboratory :

- Isolation of Native and improved Microorganisms useful towards bio-leaching. Development of Bioleaching Technology for low grade Copper ores and Uranium, to be tried at HCL and UCIL mine sites.

Scientific & Technical Achievements made:

Sixteen (16) native strains of *Acidothiobacillus ferrooxidans* and 3 Leptospirrillum isolated and characterized, Development of Highly metal resistant in these strains, Technical Protocols Chalked out with HCL and UCIL for trial of Column and Heap Leaching. Electron Microscopic, biochemical and molecular genetic studies of above microorganisms.

5. Discovery, Development and Commercialization of New Bioactive Molecules and Traditional Preparations (COR 0023)

Task assigned to the laboratory:

- Two types of tasks were assigned to the laboratory. (a) Identification and collection of medicinally important plant materials, and their extraction and fractionation for evaluation by target based therapeutics of different disease models at different CSIR labs in a networking fashion. (b) Bioevaluation of extracts obtained from plant, microbial & ISM materials as obtained from different CSIR as well as non-CSIR labs in different preclinical new-biology based target models. Under four diseases areas, namely, leishmaniasis, gastric ulcer, immunomodulation and Parkinson's disease, samples were being screened in preclinical experimental models, active samples were reexamined with repeat supply of freshly prepared samples, and selected highly active samples were identified as 'lead extract(s)' for further drug discovery exercises.

Deliverables/outcome at the completion of the project from the task/s assigned to laboratory:

- At the end of the penultimate year of X plan period, a number of leads have been generated which need to be developed further in a passage through necessary drug discovery modules. Notable among the leads are (a) two anti gastric ulcer preparations, one monoherbal and a polyherbal designed preparation, the latter one developed in collaboration with IICT, CDRI & AVS-Kottakal; (b) two anti leishmanial preparations, one in collaboration with IICT & AVS and the other in collaboration with CLRI & Siddha group, plus a few isolated active molecules therefrom which delineated the core activity; (c) one immunomodulatory principle as obtained from Siddha systems of medicine; and (d) three plant extracts that alleviated Parkinson's disease in preclinical in vivo experimental models. All these and few others in the pipeline need to be prioritized for further development towards finalizing the medicine formulation.

Scientific & Technical Achievements made:

- Development of infrastructure in terms of bioassay-guided fractionation of plant materials and isolation of bioactive molecules and delineation of molecular structures has been achieved during the X plan period.
- Likewise, development of new-biology based targeted models, appropriate for searching active samples from crude extracts in screening format, for the four major disease areas, has also been achieved.
- In terms of collection, extraction & fractionation of plant materials, so far 60 plants have been covered with about a total of 125 plant parts and about 350 number of extracts. All these were sent to 15-20 different laboratories for the evaluation of such sample in 21 disease models and around 10 pesticide-testing models. Based on feedback, a large number of extracts were fractionated and sub-fractionated, then submitted to bioevaluation laboratories.
- One lead has reached to the stage of single molecule identification and target validation under anti ulcer programme. Patent application filed and licensing to prospective industries being negotiated.
- In terms of bioevaluation at IICB, about 10,000 samples were thus far screened for anti-leishmanial and anti-*H. pylori* (under anti gastric ulcer) activities, ~ 1000 samples were screened for anti-HCl secreting potential (anti ulcer), approximately 3500 samples were examined for their immunomodulatory activity, and about 170 samples for *in vivo* anti Parkinson's activity.

6. Molecular Biology of Selected Pathogens for Developing Drug Targets (SMM-0003)

Task assigned to the laboratory :

- Studies on already identified and potential new targets of *L. donovani*
- Approaches for identification of novel targets in *V. cholerae* and *S. dysenteriae*

Deliverables/outcome at the completion of the project from task/s assigned to laboratory :

- *Leishmania donovani* : Detail molecular characterisation of DNA topoisomerases I and II, adenosine kinase, laminin-binding protein and tRNA import complex. Assay development for DNA topoisomerases I and II and adenosine kinase. Target (topoisomerase and inducible nitric oxide synthase) based chemotherapeutic assessment of several herbal and synthetic compounds.
- *V. cholerae* : Characterisation of stress response genes, functional analsysis of RelA and SpoT.
- *S. dysenteriae* : Combined physical and genetic maps of *S. dysenteriae* types 1, 2 and 7.

Scientific & Technical Achievements made :

The genes for both type I and type II DNA topoisomerases from *L. donovani* have been cloned, expressed and characterised biochemically. Individual domains of the enzymes have been identified, cloned and overexpressed proteins characterized in detail and studied for their roles in modulating the structures of the enzymes while interacting with DNA. Adenosine kinase has been cloned, expressed and characterised biochemically. By site-directed mutagenesis, a number of active site mutants have been generated and using cyclophilin dependent enzyme reactivation assay, mutants would be compared with wild type to elucidate the mechanism of Adk reaction. On preliminary screening with various ECM proteins a laminin-binding protein was found to be present on parasite surface. The protein was purified and detail molecular characterization was done like it is a 67 kD protein, it is a glycoprotein, it is an integral membrane protein, it is surface localised etc. The protein was then shown to be a transmembrane protein with a significant portion alongwith laminin binding domain oriented extracellularly, a membrane spanning domain and a c-terminal cytosolic end. The ligand binding domain was identified to be the YIGSR pentapeptide sequence present in the Zn^{2+} finger motif of B1 chain of laminin. The phenomenon of mitochondrial tRNA transport was first established in *Leishmania*. Subsequently, it was shown that translocation of tRNAs across mitochondrial membrane is a receptor mediated active transport requiring ATP. Now this tRNA import complex (RIC) has been isolated from mitochondrial membrane. The presence of constitutive NOS raises the possibility that NO-cGMP signaling may be operative in a lower eukaryote like *Leishmania*. So the presence of guanylatecyclase was looked - it has been found to be present in cytosol. As opposed to higher eukaryotes the enzyme was found to be NO insensitive and Ca^{2+} regulated. Modulation of intracellular Ca^{2+} was found to have an effect both on guanylate cyclase and parasite infectivity. The enzyme was then cloned and expressed in bacterial system. A number of compounds, both natural and synthetic and modified for antileishmanial activity has screened based on topoisomerase inhibition.

A comparative analysis of the replication origins of the large chromosomes *($oriCI_{VC}$)* of classical and El Tor biotypes of the pathogen was carried out. Effect of cold shock and stringent response in *V. cholerae* has been studied in detail. Principal stringent response regulators, RelA and SpoT, are found to present in the genome of *V. cholerae*. A combined physical and genetic map of *Shigella dysenteriae* type 1 has been constructed in his lab and comparative genome analyses indicated significant rearrangements including a 500-kb inversion in the *oriC* region of the genome of *S. dysenteriae* type 1.

7. Newer Scientific Herbal Preparations for Global Positioning (SMM-0007)

Task assigned to the lab :

- *In vivo* screening of antifungal activity *(Candida albicans)*
- Extraction and fingerprinting of five plant materials
- In vivo screening of antiparkinsonian activity

Deliverables/ outcome at the completion of the project from the task/s assigned to laboratory :

- To develop and commercialise scientifically validated herbal formulations having antifungal / antiparkinsonian activities.

Scientific & Technical Achievements made :

- Efficacy testing of other herbal extracts that are found positive in in vitro tests against *C. albicans*.
- Chemical identification of extracts for formulation etc. based on bioactivity studies
- Establishment of seasonal or local variation in contents of potential bioactive extracts
- Discovery of scientifically validated formulations or extracts for Parkinson's disease therapy

8. Developing Cell and Tissue Engineering (CMM-0002)

Task assigned to the laboratory :

- Development of hybrid cell technologies, bioengineering of melanocytes, keratinocytes, stem cell and dendritic cells for biomedical application.

Deliverables/outcome at the completion of the project from the task/s assigned to laboratory :

- Development of hybrid cells and its use for immunotherapy of leishmaniasis,
- Understanding the role of dendritic cell in leishmaniasis
- Development of cybrid technology
- Analysis of haemopoietic stem cell
- Culture of melanocytes for the treatment of vitiligo

Scientific & Technical Achievements made :

- Intellectual property rights
- Scientific publications
- Manpower development in science and Technology

9. Toxicogenomics of polymorphism in Indian population to industrial chemicals for development of biomarkers (CMM-0003)

Task assigned to the laboratory (the task assigned to the lab related only to Arsenic toxicity among all the toxicants mentioned below)

- To develop a database of the gene expression profile (fingerprints), in exposed and unexposed experimental animals, for different class of chemicals, such as petroleum products, chlorinated pesticides, bio-mass fuels, and metals (lead, mercury, arsenic, manganese etc.).
- To delineate the mode of action of the test pollutants, identify the molecular biomarkers for their exposure (key genes whose expression profile is diagnostic for the toxic response), and extrapolation of the data towards determining/predicting the toxicity of newer chemicals.
- To develop a database of the protein profile from blood, a peripheral system, in exposed and unexposed human populations, for delineation of the mode of action of the test pollutants, and identification of biomarkers for exposure.
- Development of public health data-base, related to the biological response to the environmental chemicals, and identification of individuals in the Indian population that are polymorphic in the genes, important for determining the toxic response, and accordingly are genetically predisposed to higher health risk.

- Development of human resource in the new discipline of 'toxicogenomics', by training of the scientists and students, and serve as a national resource on 'toxicogenomics' to provide facilities and infrastructure to other investigators in the country.

Deliverables/ outcome at the completion of the project from the task/s assigned to laboratory :

- Assessment of genetic susceptibility of individuals exposed to Arsenic toxicity
- To develop a database of the gene expression profile for differential susceptibility to arsenic exposure.
- Development of biomarkers
- Development of human resource in the area of 'toxicogenomics'

Scientific & Technical Achievements made :

- Arsenic exposure caused oxidation of membrane protein as evident from the enhanced formation of protein carbonyl in the red cell membrane.
- With respect to skin sensitivity, asymptomatic individuals have relatively lower sensitivity and susceptibility towards induction of genetic damage by arsenic compared to the skin-symptomatic individuals.
- Out of seven polymorphisms studied in four candidate genes (GSTT1, GSTM1, GSTP1, and GSTO1), only null genotype of GSTM1 gave significant association in arsenic toxicity and susceptibility.
- It was observed that p53 Arg/Arg genotype at codon 72 may act as a risk factor for the development of arsenic induced skin lesion (keratosis).

10. Designing Plants and Animals as Bio-reactors for Production of Proteins and Other Products (CMM-0004)

Task assigned to the lab :

- Mushrooms as a bioreactor for the production of xenogenic protein.

Deliverables/outcome at the completion of the project from the task/s assigned to laboratory :

- One patent filed, one paper communicated.

Scientific & Technical Achievements made :

- One vector has been constructed using POX promoter region of *Pleurotus ostreatus* (oyster mushroom), capable of transforming the mushroom.

11. Development of Catalysis and Catalysts (CMM 0005)

Task assigned to the laboratory :

- Development of catalysis systems in Organised Media. Design, synthesis and self-assembly of surfactants.

Deliverables/outcome at the completion of the project from the task/s assigned to laboratory :

- Two very good papers in American Chemical Society Publications.

Scientific & Technical Achievements made :

- Water Exclusion Reaction in Aqueous Media: Nitrone Formation and Cycloaddition in a Single Pot
- Stereoselective Synthesis of Chiral Oxepanes and Pyrans through Intramolecular Nitrone Cycloaddition in Organized Aqueous Media

12. Predictive Medicine Using Repeat and Single Nucleotide Polymorphisms (CMM 0016)

Task assigned to the laboratory :

- Collection of blood samples from the selected ethnic groups from eastern and north eastern India
- Preparation of genomic DNA from the biological samples
- Discovery and validation of SNPs in selected genes
- Use the data for the studies of the diseases
- Contribute to the construct of an SNP and repeat polymorphism database for the genes important in diseases and drug metabolism in the Indian population

Deliverables/outcome at the completion of the project from the task/s assigned to laboratory:

- Provide informative SNPs in genes relevant to common diseases and drug response in the Indian subpopulation
- Provide allele frequency for SNPs in the Indian subpopulations
- Create SNP database for people of India
- Manpower development, PhD thesis, publications

Scientific & Technical Achievements made :

We have collected blood samples from 15 ethnic groups from the eastern and north-eastern states of India. A large amount of data has been generated on genotypes in about 75 genes in which IICB has contributed studies on 20 genes which would give an estimate of variability of the genome in our population. The data analysis, which is in progress, is expected to unfold the level of genetic variability across population determined based on geographical location and cultural proximity reflected through different linguistic groups. The identification of SNPs in a large number of genes is in progress to identify informative SNPs in about 1000 genes in which IICB is working in 200 genes in representative populating groups of India which would be useful for studies on disease association and pharamcogenomic studies.

13. Drug Target Development using *In Silico* Biology (CMM 0017)

Task assigned to the laboratory:

- Molecular modeling of 3-D structures of proteins and their complexes with other bioactive molecules.
- Comparative genomics for identification of antibacterial/antiviral/antiparasitic drug targets
- Identification and cataloging of atypical genes & proteins in *P. falcipurum*

- To develop data mining techniques for gene expression
- To design and develop new software tools/algorithms for clustering of protein families and/or analyzing the patterns of domain distribution among these families
- Generate qualified and trained IT professionals for pursuing research in the area of bioinformatics.
- To evolve methodology for lead screening and optimization using Receptor Independent (RI) 3D-QSAR.
- To evolve methodology for lead screening and optimization using Receptor Dependent (RD) 3D-QSAR.
- To model Hypothetical Receptor Surrogate (where the receptor structure is not known) using 3D-QSAR approaches.
- Contribution in BlockII units for Mtb database.
- Human Resource Development by giving training in the area of *In-Silico* drug designing.

Deliverables/outcome at the completion of the project from the task/s assigned to laboratory:

- New software for data mining and identification of protein domains/patterns
- New computational tool for clustering of protein sequences and pathway modeling
- Scientific reports in form of publications, lecture notes, posters etc.
- 3-D structures of a number of protein-ligand systems have been studied.
- Scientific reports in form of publications, lecture notes, Invited Lectures.
- Trained professionals in the area of *In-Silico* drug designing.
- Input in Block-II units for Mtb database

Scientific & Technical Achievements made:

Novel software tools developed:

A. PROCLUST - A Protein Clustering Tool with following components :

[a] UP-Retrieve - A data mining software, written in Perl, retrieves all protein sequences available in UniProt, annotated with a particular gene ontology term.

[b] Blast-AdMat - Written in Perl, takes the Blast alignment scores and e values for all possible pairs of proteins and creates a stochastic adjacency matrix for the protein-protein similarity network.

[c] GCA - A probabilistic graph clustering algorithm based on Markov-Chain Monte Carlo simulation determines the inherent embedded cluster structure of the complex network.

[d] ClusterViz - Developed in C++ and Perl, enables integrated and segregated visualization of the protein/gene clusters with hyperlinks to their taxonomic distributions and functional annotations.

B. DomainViz - enables integrated/segregated visualization of the protein domains with hyperlinks to their functional annotations e.g. Interpro annotations and graphical views of domain architectures.

C. SPAT (Substitution Pattern Analysis Tool) - An integrated software tool for quantitative analysis of nucleotide and amino acid substitution pattrens in orhhologous genes/proteins

D. Anti convulsant drugs: A refined hypothetical receptor surface model for the allosteric receptor site, "Lactone site", on $GABA^A$ receptor based on a 3D-QSAR of N-substituted 4-amino3-3-dialkyl-2 (3H)-furanone $GABA^A$ receptor modulators has been developed. Receptor surface analysis led to the development of a highly predictive QSAR model. Findings of the study led to infer that compounds may function following "Address-Message" concept.

E. C-Jun N-terminal kinase-3 Inhibitors - as Anti-inflammatory drugs: RD (Receptor Dependent) 3D-QSAR study of benzothiazol-2-yl- acetonitrile pyrimidine core base derivatives led to the development of robust and highly predictive QSAR models which will provide clear guidelines for a novel inhibitor design based on the benzothiozole derivatives against JNK-3 for the treatment of inflammatory disorders.


BECKMAN
COULTER

Publication & Information And Planning, Monitoring & Evaluation

Drs. Alok K. Dutta, Pijush K. Das, K.P. Mohanakumar, Aparesh Bhattacharya, Uday S. Chowdhury, Moonmoon Bhaumik, Tanmoy Mukherjee, Prasanta Chakraborty, Siddhartha Majumder, Mr. Sekhar Mukherjee, Mr. Arupesh Majumder, Mr. Swadesh K. Sahoo, Mr. Binayak Pal, Mr. Nikhil K. Das, Mrs. Pratima Banerjee, Mrs. Lily Das, Mr. Sukhendu Biswas, Mr. Gopal C. Sarkar, Mr. Pallab Mukherjee, Mr. Nishikanta Naskar, Mr. Sashti Ch. Sil, Mr. Bideshi Nayak

The scientific management of the different R&D activities of the institute is the primary focus of this division. The diverse activities of this division have been carried out successfully by seven major sections, e.g. [a] Publication & Information; [b] Planning, Monitoring & Evaluation; [c] Art & Photography; [d] ISTAD-IICB; [e] Intellectual Property Management Cell; [f] Business Development Group; and [g] Human Resource Group. The details of the scientific management activities of the individual sections are given below separately for the reporting year.

PUBLICATION & INFORMATION SECTION

Dr. Tanmoy Mukherjee and group

This section is basically catering the diverse informational activities, publication and monitoring of reports. The major contribution of this section lies in assisting scientists in day to day maintenance of the institute activities and innovations, project profiles, publication records and research utilization data. The section is involved in the following wide spectrum of programmes during the report year.

- Management of Eleventh Five-Year Plan (2007 - 2012).
- Preparation of Annual Plan (2007-08) and Budget.
- Preparation of IICB Annual Report (2005-06) and half-yearly reports.
- Preparation of documents released during events.
- Dissemination of information to scientific milieu on relevant subjects.
- Documents on IICB inputs for "CSIR Annual Report" and "CSIR Research Output 2006".
- Information submitted for Custom Duty Exemption proforma for availing duty exemption by IICB.
- Assistance to scientists, fellows and staff members for participation in seminars, symposia and conferences.
- Preparation of minutes of RC meetings and other task force meetings to enable the members to follow the guidelines and proposals for future directions.
- Maintenance of database for testing and calibration.
- Total management of all technical queries.
- Public relations, advertisement and news and views forum.
- Organization display of exhibition and science news dissemination.
- Advice and comments for management of parliament queries and other related crucial matters of institute.
- Organization of 'OPEN HOUSE' and active help for 'CPYLS' programmes.

Management of Exhibition

P&I Section have participated in four (4) exhibitions during 2006-07 in and around Kolkata and also outside Kolkata organized by various organizations. The members of this section also arranged three numbers of exhibitions at IICB for different events during the reporting year. List of exhibitions are given below.

EXHIBITIONS PARTICIPATED

No.	Date	Theme	Organized by
1.	07 - 09 June, 2006	Bangalore Bio 2006	Vision Group of Biotechnology and Govt. of Karnataka held at Bangalore
2.	01 - 08 Sept, 2006	10th National Science Expo	Central Calcutta Science & Culture Organisation for Youth held at Baranagar, Kolkata - 700 090
3.	19 - 28 Jan, 2007	"Bharat Kranti Ursav"	Organised by HERITAGE BENGAL held at Rabindra Sarovar Stadium, Kolkata - 700 068
4.	Feb. 28 to Mar. 01, 2007	Science Exhibition	14th W.B. State Science & Technology Congress - 2007 held at Jadavpur University

EXHIBITIONS ARRANGED

No.	Date	Theme	Organized by
1.	April 02, 2006	IICB Golden Jubilee Foundation Day	IICB premises
2.	28-29 Dec, 2006	CPYLS	IICB premises
3.	07 - 09 March, 2007	Science Exhibition	IICB Golden Jubilee International Symposium at IICB premises

Management of Laboratory Visit for Students

On the occasion of CSIR Foundation Day (2006) celebration, the members of this section have actively helped for the arrangement of 'OPEN HOUSE' programme where students from various schools/colleges/universities within and around Kolkata visited IICB. About 393 number of students participated on that occasion. Members of this section also arranged the laboratory visit for students of outside Kolkata colleges and universities. A total of ten (10) numbers of visits were organized throughout the year (2006-07) as listed below.

No.	Date	Institution
1.	April 18, 2006	Eastern Forest Ranger's College, Kurseong, Darjeeling.
2.	May 09, 2006	Cotton College, Department of Zoology, Guwahati.
3.	May 17, 2006	KVYP fellow came from different institute in W.B.
4.	May 24, 2006	The Science Association of Bangal, Kolkata.
5.	May 31, 2006	Vidyasagar University, Kolkata.
6.	July 18, 2006	Department of Zoology, Guahati University.
7.	Oct. 20, 2006	Department of Zoology, Diphu Govt. College, Assam
8.	Dec. 18, 2006	College of Biotechnology, Birsa Agricultural University, Ranchi, Jharkhand.
9.	Jan. 05, 2007	Handique Girl's College, Guwahati - 781 001, Assam.
10.	Feb. 01, 2007	Bajkul Milani Mahabidyalaya, Purba Medinipur, W.B.

Scientist Visit & Events

The P&I Section is also responsible for the announcement and arrangement of seminars for the national and international scientists who often visit the institute and like to share their research activities with IICB faculties. A list of 'Scientist Visitors' is given in a separate page.

The Institute also organized several significant events with the assistance of this section and 'List of Events' is also shown separately for the reporting year.

Sectional Members

Dr. Uday S. Chowdhury, Mr. Sekhar Mukherjee, Mr. Arupesh Majumdar, Mr. Nikhil K. Das, Mr. Pallab Mukherjee, Mr. S.C. Sil

PROJECT MONITORING & EVALUATION SECTION

Dr. Prasanta Chakraborty and group

PME is basically involved in the management of the institute's Network as well as externally funded R & D Projects. There are fourteen numbers of Network projects and quite a few numbers of externally funded projects at IICB. Proper management of all these may lead to successful completion of those projects and steady growth of the institute. PME is also supposed to be the leading information centre of any CSIR laboratory regarding projects and therefore, PME of IICB like other CSIR laboratory is actively involved on the following activities:

- Preparation of databases for all extramural research projects (EMR) and calculation of ECF.

- Dissemination of information regarding call for National & International research project proposal / awards / fellowship and correspondences with National & International project sponsors.
- Catering to different Scientific Audit queries.
- Participation in institute's annual plan, budget preparation.
- Project expenditure monitoring of all network projects.

Sectional Members

Mr. Sukhendu Biswas, Mr. Ramdas Ravidas

ART & DRAWING SECTION

Dr. Aparesh Bhattacharya and grouup

Art Section under the supervision of Sri S.K. Sahoo has rendered full support to all the staff members during scientific seminars/symposia and all national events by preparing displays, illustrations, posters, exhibits, diagrams, charts, graphs and slides. They are working in collaboration with the Photography Section for making each exhibition a great success to highlight the institute achievements. The section also participated in preparing artwork and cover design for Hindi Day and Hindi Report and also Institute, Floor decoration and related work.

Photography Section under the able guidance of Mr. Binayak Pal has been successful in procuring a digital camera for coverage of all the events taking place in the institute. The section is continuously supplying all the photos for publications, Annual Reports, Journals and other related documents. Besides they are also assisting the scientists of the institute. Apart from that they also handled photographs of scientific activities and experiments slides for publication in different international journals.

Sectional Members

Mr. Swadesh K. Sahoo, Mr. Binayak Pal, Mr. Nishikanta Naskar

ISTAD SECTION

Diverse activities of this section were personally supervised by the Head of the Division, Dr. Pijush K. Das with the help of Dr. Moonmoon Bhowmick, Dr. Tanmoy Mukherjee and Mr. Arupesh Majumder. Some documents were also prepared for the international scientific collaboration, which are as follows :

- Management of project document on 'Cutting-edge Technology' for submission to ISTAD, CSIR
- Information on IICB for 'Contract Research' with FHG, Germany for ISTAD, CSIR
- Preparation of IICB input for 'CSIR - CSIRO (Australia) Cooperation' for ISTAD, CSIR

INTELLECTUAL PROPERTY MANAGEMENT CELL

Dr. Tanmoy Mukherjee and group

IPM Cell of IICB disseminates all information relating to patents as well as maintains liaison with scientists of IICB and Intellectual Property Management Division of CSIR. This cell is also working in close association with Business Development Group in IICB and IPMD of CSIR. In case of technology transfer and business tie-ups, the cell always provides necessary information relating to patents.

During the reporting period, Dr. T. Mukherjee had participated in some IPR related meetings and workshops as IICB representative, which are : [i] Workshop on "Negotiating Technology & Licensing Agreement" by CSIR & WIPO at New Delhi on Nov. 18-19, 2006; [ii] Workshop on IPR by IACS, Kolkata on Nov. 29, 2006. Some of the significant activities of the IPM Cell during the reporting year are as follows:

1. Maintenance of IICB Patent Database to keep it up-to-date.
2. Commercial Working Report of IICB Patents (2006) for IPMD, CSIR.
3. Renewal of 35 nos. of in force (IICB 2006) patents report sent to IPMD, CSIR.
4. Provided all necessary information for patent license agreement with M/s. East India Pharmaceutical Works Ltd., Kolkata, regarding Prostate Cancer patent to Business Development Group of IICB.
5. Made correspondence with IPMD, CSIR - 88; Response for patent applications to IPMD, CSIR - 28; Patent query of IICB scientists - 121.
6. Reply sent to Head, IPMD, CSIR regarding IICB observation on 'Protection of Intellectual Property Bill - 2007'.
7. Document prepared on total Patents of IICB filed and granted in USA for IPMD, CSIR.
8. Document prepared on patents licensed out by IICB from 2001 to April 2006 for IPMD, CSIR.
9. Information on patent and technology transfer to IPMD, CSIR regarding Parliamentary Question.

During the reporting period, 5 National Patents and 15 International Patents were filed by IPM Cell, IICB while 1 national patent and 8 International Patents were granted throughout the year.

FILED ABROAD

S. No.	Title	Inventors	Country	Date
1.	Antileishmanial activity of drug entrapped cationic liposomal formulations	Ali Nahid, Ghose Jayeeta, Bhowmick Swati	USA	25.05.06
2.	A herbal extract and herein a lupinoside as potential anti-diabetic type ii drug from pueraria tuberosa	Samir Bhattacharya, B.C Pal, Arun Bandopadhyay, Sib Sankar Roy, Swapan Kr Mandal, B.B Giri	Canada	07.07.06
3.	A herbal extract and herein a lupinoside as potential anti-diabetic type ii drug from pueraria tuberosa	Samir Bhattacharya, B.C Pal, Arun Bandopadhyay, Sib Sankar Roy, Swapan Kr Mandal, B.B Giri	Japan	10.07.06
4.	A herbal extract and herein a lupinoside as potential anti-diabetic type ii drug from pueraria tuberosa	Samir Bhattacharya, B.C Pal, Arun Bandopadhyay, Sib Sankar Roy, Swapan Kr Mandal, B.B Giri	South Africa	11.07.06

S. No.	Title	Inventors	Country	Date
5.	A herbal extract and herein a molecule, from murraya koenigii for treatment of prostate cancer	Sinha Swati, Pal Bikas Chandra, Bhattacharya Samir	World	22.08.06
6.	A pharmeceutical composition useful for the treatment of prostate cancer	Sinha Swati, Pal Bikas Chandra, Bhattacharya Samir	World	5.08.06
7.	A herbal extract and herein a molecule, from murraya koenigii for treatment of prostate cancer	Sinha Swati, Pal Bikas Chandra, Bhattacharya Samir	USA	29.08.06
8.	A pharmeceutical composition useful for the treatment of prostate cancer	Sinha Swati, Pal Bikas Chandra, Bhattacharya Samir	USA	29.08.06
9.	A herbal extract and herein a lupinoside as potential anti-diabetic type ii drug from pueraria tuberosa	Samir Bhattacharya, B.C Pal, Arun Bandopadhyay, Sib Sankar Roy, Swapan Kr Mandal, B.B Giri	China	07.09.06
10.	Leishmanicidal activity of night jasmine leaf extract containing calceolarioside a against chronic visceral leishmaniasis	Chattopadhyay Sharmila, Achari Basudeb, Poddar Avjit, Kumar Akhilesh	Nepal	09.10.06
11.	Leishmanicidal activity of night jasmine leaf extract containing calceolarioside a against chronic visceral leishmaniasis	Chattopadhyay Sharmila, Achari Basudeb, Poddar Avjit, Kumar Akhilesh	Bangladesh	09.10.06
12.	Leishmanicidal activity of night jasmine leaf extract containing calceolarioside a against chronic visceral leishmaniasis	Chattopadhyay Sharmila, Achari Basudeb, Poddar Avjit, Kumar Akhilesh	World	09.10.06
13.	Anti monocytic activity of betel leaf extracts	Santu Bandyopathyay, Bikash Pal, Samir Bhattacharya, Mitali Ray, Keshab Chandra Roy	USA	04.02.07
14.	Bioactive fraction from plant woodfordia fructicosa	Sukdeb Banerjee, Pratap K Das, Suchandra Goswami, C. Annalakshmi, Nilendu Panda, Niranjan Prasad Sahu, Basudeb Achari	World	09.02.07
15.	Bioactive fraction from plant woodfordia fructicosa	Sukdeb Banerjee, Pratap K Das, Suchandra Goswami, C. Annalakshmi, Nilendu Panda, Niranjan Prasad Sahu, Basudeb Achari	USA	12.02.07

FILED IN INDIA

S. No.	Title	Inventors	Filing Date
1.	A pharmeceutical composition useful for the treatment of prostate cancer	Sinha Swati, Pal Bikas Chandra, Bhattacharya Samir	26/04/2006
2.	A method of augmenting glut4 phosphorylation and translocation for enhancing insulin signal	Samir Bhattacharya, B.C Pal, Arun Bandopadhyay, Sib Sankar Roy, Swapan Kr Mandal, B.B Giri	24/05/2006
3.	Hybrid cell vaccine against kala-azar	Suniti Bhaumik, Rajatava Basu, Kshudiram Naskar, Syamal Roy	---
4.	Momordica charantia extract and momordicatin purified therefrom as chemothera-peutic agents against kala-azar	Salil Chandra Datta, Shreedhara Gupta, Sibabrata Mukhopadhaya	---
5.	Antileishmanial activity of Ampbotericin B entrapped in cationic liposomal formulation	Ali Nahid, Banerjee Antara	28/03/2007

GRANTED ABROAD

S. No.	Title	Inventors	Country	Grant Date
1.	Use of betel leaf extract to induce ifn-gamma production from human peripheral blood t cells and as a th1 type immunomodulator	Bandyopadhyay Santu, Pal Bikash Ch., Bhattacharya Samir, Ray Mitali, Roy Keshab Chandra	USA	16/05/2006
2.	Antimonocytic activity of betel leaf extract	Santu Bandyopathyay, Bikash Pal, Samir Bhattacharya, Mitali Ray, Keshab Chandra Roy	China	05/07/2006
3.	Two novel Gnrhs from Indian murrel brain: highly potential molecules for induced breeding of fish	Chatterjee Abhijit, Ray Partha, Dasgupta Subrata, Bhattacharya Samir	USA	11/07/2006
4.	Highly cost-effective analytical device for performing immunoassays with ultra high sensitivity	Dhar Tarun K. and others	USA	08/08/2006
5.	Herbal composition for treating asthma	Bhadra Ranjan Pal Bikash Chandra Das Krishna, Bhattacharaya Samir	Europe	13/09/2006

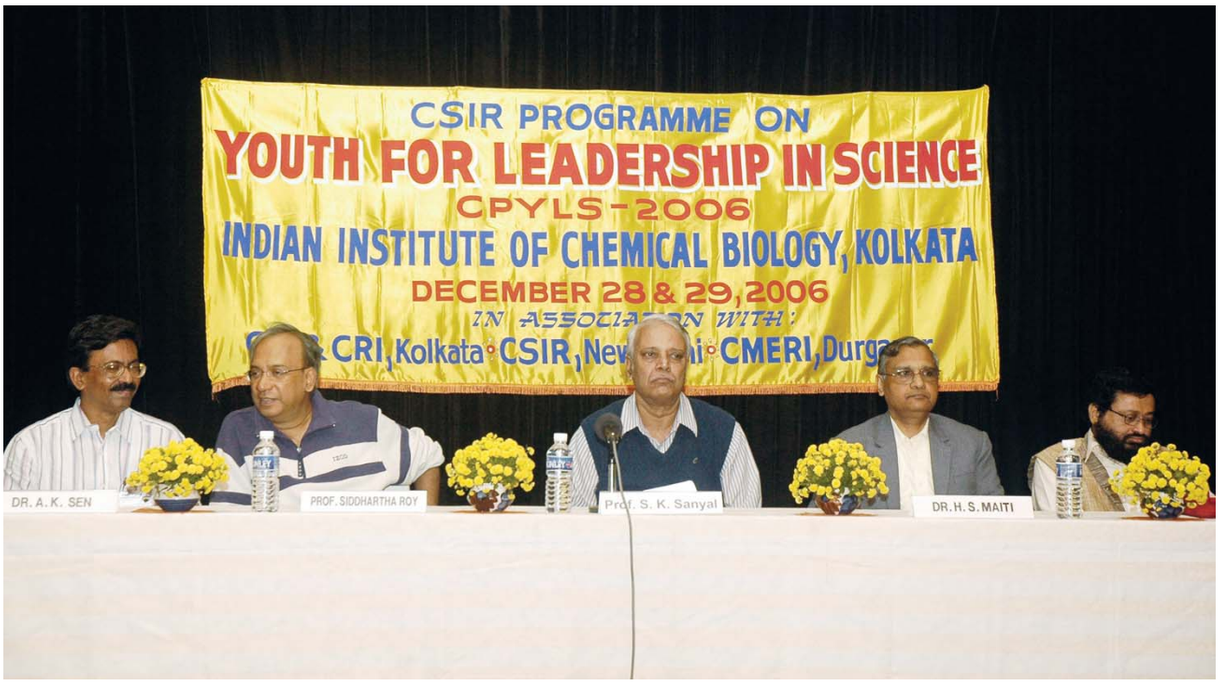
S. No.	Title	Inventors	Country	Grant Date
6.	A new cell secreting insulin	Bhattacharya S, Roy S. S., Dasgupta S, Mukherjee M	USA	31/10/2006
7.	Composition having antibacterial and antifungal properties	Bhattacharyya A. K., Pal A, Bhattacharya S	USA	05/12/2006
8.	Purified new epididymel forward motility protein and a process for isolation of the said epididymal forward motility protein useful as a fertility promoter/blocker	Gopal Chandra Majumder, Bijay Shankar Jaiswal	Europe	14/02/2007

GRANTED IN INDIA

S.No.	Title	Inventors	Grant Date
1.	A herbal medicine to treat acute and chronic myeloid leukemia	Santu Bandyopadhyay, Bikash C Pal, M Ray, K. C. Roy	17/03/2006

Sectional Members

Mr. Arupesh Majumdar, Mr. Nikhil K. Das



BUSINESS DEVELOPMENT GROUP

Dr. K.P. Mohanakumar and group

MAJOR ACTIVITIES OF THE GROUP :

[i] Liaison with pharmaceutical and biotechnology industries, CSIR, other CSIR laboratories, the West Bengal State Biotech Park, and scientists in IICB for promoting commercialization of knowhows and technologies developed in IICB.

[ii] Negotiated with clients on terms and conditions, including payment modes for finalizing transfer of knowhows and technologies developed in IICB for commercialization.

[iii] Acted as the Nodal point in IICB to closely interact with the Customer Satisfaction & Evaluation Unit, CSIR, New Delhi and provided sufficient feed back to their queries as and when asked for relating to IICB technologies, knowhows, databases, etc with close interaction with the user industries.

[iv] Submission of Service Tax returns of the institute.

[v] BDG interacted with various companies like M/s/ Tata Consultancy Services, Kolkata, Dr. Reddy's Laboratories, Hyderabad, M/s Neugen Diagnostics (India) Private Limited, Secunderabad, East India Pharmaceuticals Work Ltd., Kolkata, etc. who showed their interest to take up the technologies developed by IICB or to collaborate in R&D programs.

[vi] Liaison with CSIR regarding technologies developed in IICB and participated actively at various Forums and Events in India that are related to Bio-Business to make the presence of IICB felt.

[vii] Prepared response to all Parliamentary queries from time to time in relation to biotechnology & pharmaceutical business development activities in general, and IICB related matters in particular.

[viii] Sorted out patent related matters arising out of Grand-in-Aid projects sponsors and IICB.

[ix] BDG has tried its level best to make contacts with the industries, and initiate tie-ups with different bio-industries for successfully converting knowledge into wealth. This year IICB scientists have managed to sustain the same level of interaction with the industry and earn a considerable amount of resources both human and financial. Our partners for the overall growth towards a GATT-India regime are as follows: Neugen Diagnostics, Secunderabad; Zephyr Biomedicals, Goa; Nicholas Piramal India Limited, Mumbai; Merial SAS, Lyn, France; Dey's Medical Stores (Mfg) Ltd., Kolkata; East India Pharmaceuticals Works Limited, Kolkata; Biotech Consortium (I) Ltd., New Delhi; Shantha Biotechnics Limited, Hyderabad; Evolva Biotech Private Limited, Hyderabad; Coir Board, Kochi; Chembiotek Research International Pvt. Ltd., Kolkata and Qualpro Diagnostics, Goa.

[x] Provided wide publicity for the products available in IICB and capabilities of the institute by interacting with national and multinational agencies, press, and attending several business related meetings. Timely write-up of the institute is published in Business publications (Mohanakumar, 2006; see below).

PATENT TRANSFER AGREEMENT DURING THE REPORTING PERIOD

Sl. No.	Name of the company	Nature of agreement	Date of Agreement
1.	M/s. East India Pharmaceutical Works Limited, Kolkata	Patent license agreement for utilizing the technology in connection with the treatment and remedy of prostate cancer from herbal formulation	23.05.2006

MEMORANDUM OF UNDERSTANDING and MEMORANDUM OF AGREEMENT SIGNED DURING 2006-07

Sl. No.	Name of the Company/Institute	Nature of Agreement	Date of Agreement
1.	National Centre for Cell Science, Pune	MoU for collaborative work relating to anti-HIV activity	20.07.2006
2.	Manovikas Biomedical Research and Diagnostic Centre, Kolkata	MoU for joint research in the area of neuroactive amino acids and catecholamine metabolism	03.11.2006
3.	Manovikas Biomedical Research and Diagnostic Centre, Kolkata	MoU for joint research in the area of genomics of certain neurodevelopmental disorders	03.11.2006
4.	DBT, New Delhi	MoA for a sponsored project entitled "Identification of susceptibility alleles for the development of head and neck cancer in India"	13.11.2006
5.	DBT, New Delhi	MoA for a sponsored project entitled "Identification of new molecular targets for the development of anti-cancer agents"	13.11.2006
6.	DBT, New Delhi	MoA for sponsoring a project entitled "Development of Anti-viral agents against Chandipura virus"	16.11.2006
7.	Manovikas Kendra Rehabilitation and Research Institute for the Handicapped, Kolkata	MoU for joint research and other academic activities in the general area of Neuroscience	03.11.2006
8.	DBT, New Delhi	MoA for sponsoring a project entitled "Anti-tubercular drug design by calculated molecular descriptors: A QSAR approach"	08.02.2007

SECRECY AGREEMENTS SIGNED DURING THE REPORTING PERIOD

Sl. No.	Name of the Company/Institute	Nature of Agreement Agreement	Date of
1.	M/s. Neugen Diagnostics (India) Pvt. Ltd, Secunderabad	Test Device for rapid detection of Aflatoxin B1	18.04.2006
2.	M/s. Merial Sas, France	To exchange certain proprietory and confidential information in order to explore and evaluate the feasibility and modalities of possible co-operation for the vaccination of dogs with recombinant antigens against leishmaniasis	20.04.2006
3.	M/s. Nicholas Piramal India Limited	In connection with the know-how relating to anticancer/anti-inflammatory drugs (ICB PB 002; ICB-S003	11.09.2006

PUBLICATIONS ARISING OUT OF IICB BDG DURING 2006-07

Mohanakumar, K. P. Basic Research: The Root of Pharmaceutical Industry. West Bengal Pharma Review. Express Pharma, August 2006. pp. 33-35.

HUMAN RESOURCE GROUP

Dr. Siddhartha Majumdar and group

Human Resources Group (HRG), IICB has been set up in April 2005 to organize and nucleate Human Resources Management activities at IICB. HRG's mission is to promote professional Human Resources Management in this institute by evolving and implementing HR development plan.

Activities, Guidance and Initiatives:

- Defining & assessing institutes specific training needs and designing, developing to meet these.
- Coordinates academic & administrative affairs concerning Research Fellows/ Associates holding independent fellowship and linkages with other organization/Agencies/Institutes.
- Maintaining and updating the databases of research fellows, summer students & Academic affairs.
- Selection and placement of the summer trainees / project trainee of different post graduate students studying in different Universities, Institutions and colleges all over the country.
- Coordinate the in-house two semester PhD Course Work for the IICB PhD research fellows as a part of the academic affairs of the Institute,
- To assist in the process for nominating Scientists and Officers by the Director, IICB in different training programme / workshop [viz. R&D Management, Leadership Development and personal skills up gradation programmes etc. organized by CSIR, HRDC].
- Coordinates different awareness programme in relation to training, fellowship, etc.

Programs: Guidelines, Information & initiative

Ph.D. Programme

The major objective of this programme is to generate adequate and trained human resource in the different fields of Biology and Chemistry, and related areas for meeting the requirement of cutting edge research. The duration of this programme is generally five years.

Eligibility criteria

For admission to the PhD program of the institute, the CSIR-NET qualified candidates / UGC-NET / ICMR fellows / DBT fellows can directly join the institute in their area of interest subject to consent from the institute's faculty to be the candidate's supervisor and director's approval.

Junior Research Fellowship for GATE qualified engineering graduates (CSIR JRF-GATE)

CSIR has introduced a new research fellowship in 2002 for the GATE qualified candidates with B.E., B.Tech., B.Arch, B.Pharm. degree to pursue research leading to Ph.D. Each CSIR laboratory engaged in biological/biochemical research can have maximum 10 such JRF-GATE fellows.

Besides the adhoc fellowship, IICB advertises for recruiting research fellows to work in grant-in-aid projects and different research schemes.

At a Glance: Research Fellow

Number of Research Fellows :

- CSIR Research Fellows (JRF+SRF): 93
- CSIR Research Associate (RA): 10
- UGC Research Fellows (JRF+SRF): 20
- ICMR Research Fellows (SRF+RA): 14
- DBT Research Fellows (JRF): 04

Career Opportunities: Research / Training

Ph.D. Course Work

The HRG & Academic affairs Committee has been organizing PhD course work, offering two-semester course work. The main objective of this course is to make them acquainted with modern modern biological sciences, chemistry and chemical biology. The course is mandatory for students registering for Ph.D. degree. The duration of this course is normally 120 hours. The course comprises of two major disciplines, namely Basic Course with [a] Computer Applications; [b] Instrumental Analysis; [c] Statistical Analysis; [d] Basic Biology (for Chemistry students); and [e] Basic Chemistry (for Biological Sciences students); and Advanced Course with [a] Advanced Biology (for students engaged in Biological Sciences Laboratory) and [b] Advanced Chemistry (for Chemistry Laboratory students).

Summer Training / Project Work / Dissertation Work

The Human Resource Group, IICB provides an excellent environment for training the next generation of researchers and is proud to support training towards partial fulfillment of the respective postgraduate degrees. IICB has imparted training in the state-of -the-art techniques to several summer students from different universities & Institutes. The aim is to let young minds feel the thrill and excitement of science by working on a project requiring application and critical appreciation of scientific principles. It also aims at active participation in the learning process through experimentation and putting into practice the knowledge acquired in the classrooms.

Students pursuing M. Sc./M. Tech./M. Pharm. etc. from various universities/institutes of the country get short-term training in different laboratories of this Institute. Under this programme the Institute conducts training of short duration in various disciplines and is absolutely free of any cost. The courses comprise both lectures and practical with emphasis on practical R&D aspects in a particular discipline. The duration of this training programme / Project Work is generally two- three months and maximum six months duration during March and August every year.

Year 2007: Number of Summer Trainee, Project Trainee, Short term-trainee: **110**

Other Activities and Initiatives: Nomination in Training & Workshop

To assist in the process for nominating Scientists and Officers by the Director, IICB in different training programme/workshop [viz. R&D Management, Leadership Development and personal skills up gradation programmes etc. organized by CSIR, HRDC.

Participants in Training/Workshop:

- Sri Arghya Basu, SRF, UGC participated in the "4th Technology Led Entrepreneurship Training Programme for research scholars" organized by CSIR, HRDG in collaboration with CLRI, Chennai during Feb.12th to March 11th 2007 at CLRI, Chennai.
- Dr. Aditya Konar, Scientist and Dr. Subrata Adak, Scientist participated in "Development of Managerial Efficiency for Scientist" programme during 12th March to 16th March 2007 organized by HRDC, CSIR & Fore School of Management, New Delhi at HRDC, Ghaziabad.
- Dr. P. Jaisankar, Scientist participated in the" Decision Support Tools and Techniques for senior scientists" organized by DST, GOI during 2nd April to 6th April 2007 at ASCI, Hyderabad.
- Dr. Mrinal K. Ghosh, Scientist participated in special training programme on " Enhancement of Managerial Efficiency for Scientists" during 4th to 8th June 2007 organized by HRDC, CSIR at HRDC, CSIR, Ghaziabad.
- Dr. Malini Sen, Scientist participated in "Induction Training Programme for newly recruited Scientist" during 20th to 25th August 2007 organized by HRDC, CSIR at HRDC, CSIR, Ghaziabad.
- Dr. Siddhartha Majumdar, Technical Officer Gr-III (6) & Head, HRG participated in "Workshop on Strategic Management of Human Capital" organized by the HRDC, CSIR during 12th to 14th Oct 2007 at Ghaziabad.
- Dr. M. C. Bagchi, Scientist participated in "Training Programme on Research Methodology and Statistical Methods" held during 17 - 20 September, 2007 organized by HRDC, CSIR at Ghaziabad.

Training/ Programme arranged in IICB

- For Jagadis Bose National Talent Search (JBNSTS) Scholars (16 nos.) Lab Visit & meet the scientists" programme was coordinated on 18-07-2007.
- Scientific Awareness Programme for IICB PhD Students (female), executed by Cancer Foundation of India has been arranged at IICB
- M.Sc. Biotechnology students (35 nos) of St. Xavier's College, Kolkata have learnt confocal microscopy & phase contrast microscopy on 8th October 2007 under the guidance of Dr. Samit Adhya, Scientist.
- During the year 2006, the HRG, IICB, had conducted computer literacy training programme in DOECC Center, Jadavpur University Campus for 15 IICB technical, administrative, finance and purchase staff members working in different dept./section.

Sectional Members

Ms. Lily Das, Ms. Pratima Banerjee, Sri. B. Nayak

Computer Division

Mr. Debashis Paul, Dr. Asoke Dasgupta & Mr. Ashutosh Mukherjee, Mr Prahlad Das

Technical Support:

i) Upgrading Existing IT Facilities at IICB

CSIR has taken up the task of "Building a Scientific Knowledge Grid, ICT Infrastructure & Services for CSIR laboratories CSIR". In order to upgrade the existing IT facility, under the budget head ICT infrastructure and Services, a sum of Rs. 215.00 Lac has been allotted to IICB. During 2006-2007, IICB has received Rs. 125.64 lacs, which has been utilized for upgrading the existing IT facilities. Under this budget head, two high-end servers, latest UPS and an integrated hardware unit for IICB Internet security management have been procured. Besides these, 200 desktop PCs, laptops, printers, etc. have been procured and distributed to the scientists. About 50 new Internet connections have been installed; with CAT 5 cables and wireless access points. We are planning to implement wireless technology for future expansion of IICB LAN.

ii) Maintenance, Supervision, Monitoring, Extension & Updating of IICB-Internet Facility

IICB-Internet-Facility presently comprises of Router, Modem, seven servers, more than 12 network switches, 400 nodes, etc. Network security software like Firewall, Intrusion Detection software, anti-virus software (for 200nodes) etc. has been installed to protect IICB resources.

This Division looks after about **400 nodes** with various problems, like network problem, PC level problem etc., Partial repairing, maintenance and system configuration (installation of network driver card) of in-house computers are undertaken on regular basis. All hardware and software related works are undertaken on need basis.

IICB Web Site has been modified from time to time on regular basis. On line status of the IICB Scientific Activities are now available in IICB web site, which also supports on line registration for symposium etc. Facilities for press tender and press advertisement for fresh procurement and fresh recruitment have been introduced in the IICB web site. Besides this, an Intra-web-site has been introduced for internal matters and internal users only, which include various types of purchase procedures, indent forms for purchase, Administrative matters, internal office Memos/ news etc. The Intra-web-site is updated from time to time on regular basis.

iii) Software Support

Computer Division provides software supports to Administration Sections as and when Required (e. g. Income Tax Calculation for Bill Section).

iv) In-house Computer Training

Like every year, this year also, this Division has organized Introductory Course on Computer in Biology for research scholars. About 60 students participated in this in-house training course.

Scientific Activities/ Achievements

With the financial assistance of the Department of Scientific Technology (DST, Instrument Development Programme), a computer based instrumental system, the SPERMA (sperm motility analyzer), has been developed

to determine sperm motility, using a spectrophotometer for clinical and biological applications. In order to acquire the intellectual property right, this unique work has already been filed for National. Indian Patent Application File No. 1605DEL2004 Dated: 26.08.2004.

The SPERMA is altogether a special kind of spectrophotometer, capable of positioning the cuvette vertically in four different heights, and thus exposing the spermatozoa solution in four levels of light paths. As a result, it is possible to generate four or more sets of data at a particular time and thus it is capable to determine sperm motility more accurately for the entire spermatozoa sample. The idea of vertical movement of the cuvette in a spectrophotometer is altogether a new and unique conception. There is no spectrophotometer available in the world, in which cuvette is movable vertically in upward and downward directions within the light path. Again there is not a single instrument, which considers vertical movement of the sperm cells in determining motility parameters. This instrumental system has got great commercial uses for the human fertility clinics, various research Institutions/ Organizations, various animal and cattle breeding centers in rural and urban areas etc. International Patent Application File No. is 0261NF2004/WO - PCT/IB05/02541, Dated: 26.08.2005.

Individual Group Activities With Participant's Names

But, the above-mentioned instrumental system, the SPERMA, is capable of measuring motility of a single sample only at a time. In order overcome this limitation and also for the purpose of calibration and standardization, a new project has been submitted to the Department of Scientific Technology (DST, Instrument Development Programme) for financial grant.

Calibration and standardization are the two important terms that determine the quality of an Instrument. Thus, various tests have been conducted using SPERMA for goat cauda epidemic with inhibitors and activators. Using same samples, simultaneous tests have also been conducted on SPERMA and CASA. When data are compared, comparative results observed to be of the similar trends, though CASA measures parameters in horizontal plane. Again there is not a single instrument, which considers vertical movement of the sperm cells in determining motility parameters with which SPERMA-data could be compared. Thus, in order to standardize, SPERMA needs several tests with various cells of various species, including human serum, of known and standard motility parameters. Samples of known motility are to be collected from various, hospitals, fertility clinics, animal husbandry etc., and conduct experiments with SPERMA and analyze the comparative results.

The main purposes for submission of the new project is planned to calibrate and standardize this unique instrumental system, SPERMA, and correlate the vertical motility parameters experimentally with fertilizing ability of the spermatozoa. The other purpose of this project is to upgrade the SPERMA by incorporating multi-cuvette (multi-sample) and multi-height exposures of the spermatozoa samples. The present instrumental system, which is capable of testing only for single sample and multi height exposures, needs modifications to improve the usage and utility. Extensive studies have been conducted for this purposes.

Publications

i) Saha S., Paul D., Mukherjee A., Banerjee S., Majumder G. C.: A computerized spectrophotometric instrumental system to determine the "vertical velocity" of sperm cells: a novel concept. *Cytometry Part A.*

External Funding

A Scientific Project has been submitted to the Department of Science & Technology, IDP Division, New Delhi, for a financial assistance of Rs.14,89,600.00. A brief details of the project has been given in group activities above.

Honours and awards

International Award:

Saha S., Paul D., Mukherjee A., Banerjee S., Majumder G. C. (2007): Measurement and Analysis of Vertical Motility of Spermatozoa with Special Reference to Vertical Velocity. (Abstract): Sudipta Saha, Senior Research Fellow, received "Biotech Idea to Innovation Award 2007" from British Council, New Delhi, India, for the development of this unique instrumental system. In connection with this award, Mr. Saha has been invited by the British Council to visit and get exposure to modern research technologies of UK laboratories at Oxford University and Brunel University for a month.

Best Poster Award

Sudipta Saha, Debashis Paul, Ashutosh Mukherjee, Somnath Banerjee, And Gopal Chandra Majumder. Development of a unique computerized spectrophotometric instrumental system to determine "vertical velocity" of spermatozoa for clinical and biological applications. In International congress on gamete biology: emerging frontiers in fertility and contraceptive development, 22 - 25 february, 2006, national institute of immunology, new delhi. Poster no. **6**, Pg. 48.

Members Of Scientific/ Technical Committees

i) Mr. D Pal has been nominated as one of the members of the Assessment Committee by Central Glass & Ceramic Research Institute, Kolkata.

ii) Mr. D Pal has been nominated as one of the members of the Assessment Committee in Central Glass & Ceramic Research Institute, Kolkata, for Gr. (I), Gr. IV(2), Gr. IV(3), Gr. (4)

iii) Mr D Pal has been nominated as one of the members of the Internal Screening Committee in Indian Institute of Chemical Biology, Kolkata, for Gr. IV(2), Gr. IV(3), Gr. (4).

iv) Mr D Pal is selected as a question Setter in Assam University, Silchar, P. G, Biotechnology: in "Computer Applications & Biostatistics".

v) Mr D Pal is selected as an examiner (evaluation of answer scripts), Assam University, P. G, Biotechnology: in "Computer Applications & Biostatistics".

vi) Dr Asoke Kumar Das Gupta is nominated as a committee member of Management Council at IICB.

vii) Dr Asoke Kumar Das Gupta is nominated as a Advisory Committee Member of IICB in connection with setting up of National Institute of Pharmaceuticals, Education & Research (NIPER) at Kolkata.

Library & Documentation Division

Mr. N. C. Ghosh, Mr. S. K. Dey, Mrs. P. Chatterjee, Mr. S. Bhakta, Mr. S. K. Naskar Mr. A. M. Dhank, Mrs. S. Ganguly, Mr. P. K. Das, Mr. T. K. Mukherjee, Mr. M. Halder, Mr. S. Nath, Dr. B. K. Ghosh

The Library and Documentation Division has been marked the remarkable growth in respect of collection, systems, facilities and services during the period under review. The services rendered from the division are like reading room facilities, on-line and off-line literature search information services through CD-ROM database - ADONIS, lending facility, reference and referral services, reprographic and resource sharing etc. On-line availability of the journals of High Impact Factor through CSIR E-Journal Consortium enhanced the services tremendously. The division has LibSys 4.0 software installed on Linux (Fedora-core-4) platform for facilitating access to the library catalogue through Web-Opac. The computerization programme of the division is on the way in full swing.

The division is basically to provide library information services to the S & T personnel, staff members, research scholars and others associated with the Institute. However, outside users like academicians, bonafide research scholars, bonafide students etc. are also allowed to make use of Library information services.

Collections	**2006-2007**	**Total**
Books including Hindi Books (OLIC)	377	12656
No. of Titles of Journals (including titles on-line of SD, Springer, Blackwell, ACS, John Wiley, OUP, RSC, Taylor & Francis, Emerald, Nature, Cell Press, Science & CSIR e-journal consortium)		4600
Bound Volumes of Journals	795	30474
Annual Reports	47	3761
Monographs(including WHO monographs)	14	2051

Services	
ADONIS Printers	1523 articles (approx.)
ADONIS Searches	179 articles (approx.)
Reference Queries	1155
Resource Sharing	75
Photocopying	26,400 pages (approx.)
Journals (issued/returned)	6406
Books (issued/ returned)	8584
Users from outside	1932
Online Journal Access	3702 Users

Instrumentation Division

Dr. S.K. Dana, Mr. T.K. Mukherjee, Mr. Kalyanmay Datta, Mr. U. Halder, Mr. S. M. Roy, Mr. A. K. Pramanik, Mr. T. P. Nandi

The Central Instrumentation Division takes care of the repair and maintenance of all scientific instruments of the institute. In addition, the division is actively involved in developing the infrastructure and basic amenities for major equipments of the institute. The division supports the operation of Centrifuge, Ultracentrifuge, UV/VS spectrophotometers and Lypholyzer. The regular maintenance support is provided on small and essential instruments which are of high demand like fraction collector, electrophoresis apparatus, high voltage power supplies, voltage stabilizer and high vacuum systems to mention a few. The division also supports the audio-visual systems, video conferencing system in the institute during several meeting, seminar and conferences held throughout the year. Moreover, in recent years, the division initiated R&D efforts on developing new biomedical equipments and on experimental chaos synchronization in electronic circuits.

A group of scientists, technical officers and skilled technicians assist in the operation, repair and maintenance of scientific instruments used by different group in life science and chemistry of the institute. A few research scholars are working towards Ph.D. degrees on different theoretical and experimental aspects of nonlinear dynamics, data analysis.

Research and Development

Research and development have been initiated in the instrument division with the purpose of developing new apparatus for biological research and also for developing new understanding of natural systems like, biological and physical. Nonlinear dynamical approach is mainly targeted to understand living system behaviors like cardiac arrhythmia, neuronal interaction in the brain under pathological condition. Trends of research are set around the world in recent years to understand these aspects using concept of synchronization in nonlinear oscillators and complex networks. The focus of our current research is to develop understanding of some of these aspects through studies on synchronization of coupled chaotic electronic oscillators and paradigm models. The basic idea is to set a trend of interdisciplinary research bringing together the knowledge of physics, electronic and biology to explore complex dynamics of natural systems.

A few fundamental aspects of chaos synchronization, namely, anomalous phase synchronization and phase flip bifurcation have been explored and their experimental evidences in electronic circuits are reported for the first time in highly peer-reviewed journals. Attempts are being made to set up animal experiments and data analysis to investigate rat's brain function under drug-induced condition in collaboration with the neurobiology group of the institute.

National and international collaborations have been established. Some of the premier institutions in the country like Presidency College, Kolkata; School of Physical Sciences, JNU, New Delhi; Department of Physics and Astronomy, Delhi University; Institute for Plasma research, Gandhinagar, Gujarat, are participating in joint research. Institution from abroad like the Institute of Physics, University of Postdam, Germany; Department of Mathematics and Computer Sciences, Elizabeth State University, North Carolina, USA; Institute of Physics, Academia Sinica, Taiwan started collaboration on nonlinear dynamics research.

Research Fellows

Mr. Ranjib Banerjee

Mr. Sourav Bhowmick

Extramural Research Activities

An ongoing project on chaos synchronization is supported by the DST for the years 2006-2009.
An international collaboration between IICB and University of Medicine and Pharmacy, Iasi, Romania has been initiated on control and synchronization of chaos.

Invited Lectures

"Experimental evidence of Phase flip bifurcation", Institute of Physics, Academia Sinica, Taiwan.

"Phase flip bifurcation: Theory and Experiment", School of Physical Sciences, Jawaharlal Nehru University, New Delhi

External Funding

Principal Investigator	:	Dr. Syamal Kumar Dana
Co-Investigators	:	Dr. Prodyot Kumar Roy, Department of Physics, Presidency College, Kolkata
		Prof. Abhijit Sen, Institute for Plasma Research, Gandhinagar, Gujarat
		Dr.Gautam Sethia, Institute for Plasma Research, Gandhinagar, Gujarat
Project Title	:	Synchronization nonlinear systems: Theory and Experiment
Funding Agency	:	Department of Science and Technology, New Delhi
Total Fund	:	16.76 lakh
Duration	:	2006-2009

Honours and Awards

Reviewer of International Journals: Chaos, Pramana-J. Physics, Physics Letters, European J.Physics, Int. J.Bifurcation and Chaos.

Publications :

1. Prasad A., Kurths J., Dana S.K., Ramaswamy R. Phase-flip bifurcation induced by time delay. *Phy.Rev.E* **74**: 035204(R), 2006.

2. Dana S. K., Sengupta D. C., Hu C-K., Spiking and bursting in Josepshon junction. *IEEE Trans. Cir.Systs-II: Express Briefs* **53** (10): 1031-1034, 2006

3. Dana S. K., Roy P. K., Sethia G. C., Sen A., Sengupta D. C., Taming of chaos and synchronization in RCL-shunted Josephson junction by external forcing. *IEE Proc.Circuit Devices and Systs*. **153** (5): 453-460, 2006

4. Roy P. K., Dana S. K., Gluing bifurcation in Chua oscillator. *Int. J. Bifur. Chaos* **16**(12): 3497-3508 (2006).

Animal House

Dr. A. Konar, Mr. H. Ray, Mr. S. S. Verma, Mr. R. K. Sarkar, Mr. A. Das, Mr. J. Middya, Mr. P. Middya, Mr. T. Sarkar, Mr. A. Sardar, Mr. G. C. Mondal

IICB with its CPCSEA registered animal facility (Registration No 147/1999/CPCSEA) is identified as a key-organization for biomedical research. There are a number of projects where laboratory animals are used as a basic tools. All (animals) but a few special strain of mouse, are being supplied from the in-house breeding colony. Moreover, some other research institutes who have their CPCSEA registration, also collect animals from the facility for their IAEC approved research projects.

The animals are produced and kept in a scientifically maintained environment (Room Temp. 24 ± 2°C ; relative humidity 55 - 60%; light and dark schedule 12:12hrs; illumination 350-400 lux at 1 mt above the floor, and 10 - 12 air-cycles/hr). The house keeping of the facility acclaimed high appreciation not only from the associated scientists but also the representatives of CPCSEA, representative of different NGOs and private entrepreneurs, distinguished scientists, etc. who visited the facility during this period.

Animals (specially mouse) were purchased from other registered breeders only when the required strain was not available in the colony or when animals of same specification was required in a bulk. However, proper utilization of animals was strictly monitored and animals were produced in such a number, that the number of unutilized animals be minimum but the scientists get their animals as and when they require. A brief account of animal produced/supplied from the animal house in the last year is given in the following table :

Species	Stock on 1st April 2006	No. of animals		Total (A)	No. of animals issued		No. of animals		Total (B)	Stock on 31.3. 2007 (A-B)
		Produced	Purchased		Produced	Purchased	Died in-stock	Supplied to other R&D organi-zations		
Mouse	2543	5068	165	7776	5259	165	225	25	5674	2102
Rat	2626	3631	0	6257	4274	0	0	67	4341	1916
Hamster	255	1770	0	2025	1722	0	0	0	1722	303
Rabbit	101	44	0	145	35	0		08	43	102
Guinea pig	31	0	0	31	0	0	6	0	05	26

Engineering Services Unit (ESU)

Dr. J. Rajan Vedasiromoni, Mr. D. P.Das, Mr. U. K. Barua, Mr. S. Saha, Mr. S. Ray, Mr. B. Jayakumar, Mrs. N. Bage, Mr. U. B. Sarkar, Mr. D. Banik, Mr. S. Basak, Mr. M. B. Malakar, Mr. G. Malik, Mr. D. K. Ghosh, Mr. S. N. Mondal, Mr. S. Pradhan, Mr. S. Biswas, Mr. S. R. Tudu, Mr. S. Nath, Mr. S. Mazumder, Mr. A. Pal, Mr. B. Das.

The Engineering Services Unit (ESU) is comprised of the Civil Engineering, Electrical and Air-conditioning & Refrigeration sections.

i. Civil Engineering section:

The Civil Engineering Section renders service in the broad areas of infrastructural development, renovation of laboratories & common facilities, maintenance of sewerage and drainage systems and disposal of biological including radioactive waste.

List of major works in the past one year:

1. Repair, renovation & up-gradation of laboratories.
2 Rectification of seepage in lift pit.
3. Repair, renovation & up-gradation of Toilets
4. Renovation of canteen

The following Civil & Structural Engineering works are in progress or in proposal stage:

1. Renovation of stores & Administrative section.
2. Emergency exit staircase connecting all floors of IICB main building for fire exit in case of fire.
3. Replacement of pipe lines and corroded steel tank.
4. Repair & renovation of water proofing treatment of roofs of auditorium and library.
5. Construction of new central AC plant
6. Structural repair of overhead water tank.
7. Renovation of car shed for new canteen & construction of scrap materials shed.
8. Renovation of auditorium.

ii. Electrical section:

The Electrical Section renders essential services and infrastructure support to R & D activities and other public utilities of the institute. The section also maintains and supplies steady power supply through 2 MVA power sub-station and monitors uninterrupted power supply system from CESC source as well as emergency power through available DG - sets including its operation and maintenance.

List of major works in the past one year:

1. Provision of emergency power points through 60 KVA DG set to different laboratories in the 2nd and 3rd floors of the institute.

2. Renovation of electrical installations in various rooms including library and administration.
3. Provision of grounding system for newly installed 160 KVA DG set of BSL-III facility.
4. Preventive maintenance of 2 X 1000 KVA power transformers.
5. Improvement of illumination system in the institute premise and corridors.
6. First phase of energy audit to review conservation of electricity through CSIO Regional Center, Chennai.

The following electrical works are in progress or in proposal stage:

1. Improvement of power supply system.
2. Renovation of LT power distribution system of sub-station.
3. Renovation of electrical installation in lift room and some laboratories.

iii. Airconditioning and refrigeration section:

This section looks after the AC facility in all the laboratories, library, auditorium, administrative wings and most importantly the animal house. It also takes care of the refrigerators and deep freezers in the laboratories, maintains the cold rooms and constant temperature rooms and is responsible for the maintenance of the lifts.

List of major works in the past one year:

1. Installation of split AC units in laboratories.
2. Annual maintenance of window and split AC units.
3. Annual maintenance of 80TR AC plant for animal house
4. Annual maintenance of 3 x 7.5TR package unit for administrative wing.
5. Maintenance of cold rooms.

The following works are in progress or in proposal stage:

1. Modernization of passenger lift near the canteen.
2. New installation of 200TR chiller plant with piping and ducting for auditorium and library.

Architect Engineering Services Unit

Mr. S. Basu, Mr. S. Ghosal.

The unit is totally devoted to the development, planning and construction in the new campus measuring 4 acres in Salt Lake.

Administration

The Administration takes care of the day-to-day activities required for smooth functioning of the Institute. The Administration is divided into three Divisions :

A. GENERAL ADMINISTRATION

General Administration comprises of the following Sections :

[i] *Recruitment & Committee*

This Section takes care of the recruitment and promotion of all Scientific, Technical and Administrative staffs. It also arranges for engagement of Project Assistants for different projects.

[ii] *Establishment*

This Section maintains the personal files of all the employees of the Institute.

[iii] *Bill & Cash*

All works related to preparation of salary bills and other advances as well as disbursement of cash are taken care of by this Section.

[iv] *General Section*

This Section takes care of all miscellaneous types of work including Works & Services.

[v] *Vigilance & CR Cell*

This Section keeps a vigil eye on all activities of the Institute. The confidential reports of all the employees are also maintained by this Section.

[vi] *Legal Cell*

The Legal Cell takes care of all legal activities related to the functioning of the Institute.

[vii] *Security*

The safety & security aspects of the Institute are taken care of by this Section.

B. FINANCE & ACCOUNTS

This Division takes care of all financial matters of the Institute which is of the tune of more than Rs. 20 crores per year.

C. STORES & PURCHASE

This Division takes care of purchase of materials from the country as well as from abroad.

Official Language Implementation of the Institute

The Official Language Implementation in this Institute has been improved remarkably in the last year. Many employees have passed the Praveen and Pragya the year 2006.

On 25th July 2006 two Hindi workshops on rules and regulations of Hindi language implementation were held and on Hindi spellings and grammer which was conducted by Smt Sushmita Bhattacharjee, Research Officer and Smt Dipti Ghosh, Asstt Director respectively both of the Official LanguageTeaching Scheme, Home Ministry Kolkata.

Apart from these activities, Hindi week was celebrated from 11 to 14th September 2006 wherein many competitions and Hindi workshop on Hindi implementation were held. Sri Avdesh Prasad Singh, Sr Hindi Officer UCO Bank conducted this workshop. Sri Prem Shankar Tripathi, Proffesor of Hindi in Surendranath college was invited as the Chief Guest on the occation of Hindi Day on 14th September. Dr Anup Bhattacharya, Sr Scientist of the Institute presided over the programme Sri R. S. Gupta, Hindi Officer of Indian Oil Corporation & Sri Vijay Shankar Misra, Hindi pradyapak were the judges of various competitions like Hindi noting drafting, essay, recitation competitions. The Administrative officer of this Institute Sri SK Chaudhury proposed the vote of thanks.

Smt. A. Nag, Sr Hindi Translator organized these programmes.

Scientist Visitors

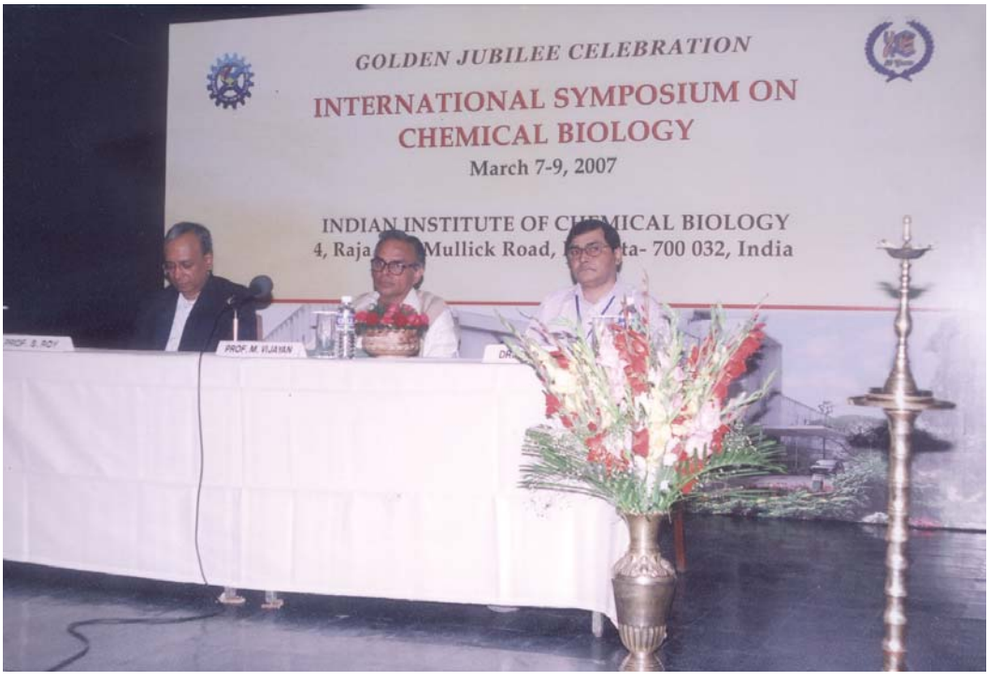
No.	Date	Speaker	Title of Seminar
1.	11.04.2006	Dr. Jayati Sengupta, Univ. of Albany, USA	3D Imaging of the Ribosome: Cryo-EM as an Investigative Tool.
2.	17.04.2006	Dr. Surojit Paul, Univ. of Albuquerque, USA	Neuronal signalling through tyrosine phosphatases, one STEP at a time.
3.	18.04.2006	Dr. Surajit Sinha, Stanford Univ., USA	Synthesis of caged morpholines and its applications in spatiotemporalcontrol of zebrafish gene expression.
4.	02.05.206	Dr. Mahua Ghosh, USA	Nui inhibits the Anabaena nuclease NucA through target site mimicry.
5.	17.05.2006	Prof. Dipankar Chatterjee	Some thoughts on KVPY.
6.	07.06.2006	Dr. Sunil Kr. Mandal, Tuscon, Arizona, USA	Organometellics asymmetric catalysis, total synthesis and medicinal chemistry: never ending journey of a chemist.
7.	15.06.2006	Dr. Shankar Guchait, Birla Inst. of Tech., Goa	Organic synthesis and drug discovery.
8.	21.06.2006	Dr. Dinabandhu Naskar, Chembiotech, Kolkata	Combinatorial chemistry for drug discovery.
9.	03.07.2006	Dr. Mahadeb Pal, Cleveland Clinic Foundation, Ohio	Understanding promoter clearance by RNA polymerase II.
10.	18.07.2006	Dr. Amit Mandal, IISs., Bangalore	Application of mass spectrometry in de novo sequencing of peptides and in search for clinical markers of oxidative stress
11.	20.07.2006	Dr. Tapan Mukherjee, Univ. of Utah, USA	Role of glutathione-dependent reductive strees in controlling pro-inflammatory proteins.
12.	25.07.2006	Dr. Kamal U. Saikh, USAMRIID, USA	Innate immune regulation and anti-inflammatory drug target.
13.	27.07.2006	Dr. Sudha Sharma, National Inst. of Health, USA	Genomic instability and cancer : insights from analyses of Rec Q helicases
14.	02.08.2006	Dr. Alakananda Hajra, Visva Univ., Shantiniketan	Asymmetric Synthesis: The key of New Drug Discovery.
15.	14.08.2006	Dr. Tapas Sen	Nanobiotechnology research in Europe: development of nanomaterials, surface engineering and their applications in biosciences.

No.	Date	Speaker	Title of Seminar
16.	27.10.2006	Dr. Ruchi Anand, Univ. of Pennsylvania, USA	Structural and Functional Implications of Domain Organization in the Purine Biosynthetic Enzyme Formylgycinamide Synthetase.
17.	06.11.2006	Dr. Prabhat Arya, Steacie Institute, Canada	Natural product-like probes-Small molecule microchips: Emerging tools aimed at dissecting signalling networks using small molecules.
18.	07.11.2006	Dr. Abhijit Mukhopadhyay, Purde Univ., Indiana	Import of proteins into Mitochondria.
19.	14.11.2006	Dr. Mahesh Patil, Osaka Univ., Japan	Asymmetric synthesis using chiral spiroligands and immobilization of Enantioselective catalysts.
20.	22.11.2006	Prof. Aryan Namboodiri, USUHS, Bethesda, USA	Canavan Disease : Neurochemical defects and treatment.
21.	24.11.2006	Dr. Jayanta Mukhopadhyay, Rutgers Univ., USA	Transcription : Structure and Mechanism.
22.	30.11.2006	Dr. Biplab Dasgupta, Washington Univ. School of Medicine, Saint Louis, USA	Neuronal Energy, Health and Longevity: Elucidating the functions of an ancient cellular fuel guage.
23.	20.12.2006	Dr. Satish Sankaran, Harvard Medical School, Boston, USA	Role of BRCA1 in regulation of centrosome duplication and function.
24.	22.12.2006	Dr. Raghu K Chitta, Univ. of Virginia, USA	Mass Spectrometric Methods to Study Proteins : Post-Translational Modifications and Self-Association Interactions.
25.	10.01.2007	Prof. Subhash C. Basu, Univ. of Notre Dame, USA	Activation of Proteases in Apoptosis and Inflammation.
26.	10.01.2007	Dr. Subhash C Biswas, Columbia Univ. USA	Neuronal apoptosis in development and disease : role of a death-associated gene.
27.	16.01.2007	Dr. Dhruba K Chattoraj, Head, Control of DNA Replication Section, NIH, Bethesda, MD	Chromosome Dynamics in Vivrio Cholerae
28.	17.01.2007	Dr. Santanu Dasgupta, Johns Hopkins Cancer Research, Building, North Baltimore, USA	Role of Mitochondria ecoded cytochrome B gene mutuation in bladder cancer.
29.	24.01.2007	Dr. Soma Banerjee, NIH, USA	The ELH1 replicating factor C like complex: a novel guardian of genome instability

No.	Date	Speaker	Title of Seminar
30.	01.02.2007	Dr. Balaram Mukhopadhyay, CDRI, Lucknow	Glycobiology-chemist shake hand with biologist.
31.	07.02.2007	Dr Nakul C Maiti, Case Western Reserve Univ. USA	Biophysical Studies of a-Synuclein and its Aggregates Associated with Parkinson's Disease and other Biophysical Synucleinopathies.
32.	09.02.2007	Prof. Charles L. Jaffe, Herbew University	Studies of a Schizopherenic Leishmaniac : Protein Kinases and Parasite Diagnosis.
33.	14.02.2007	Dr. Saubhik Halder, Jadavpur University	A physical bio-organic approach of membranemimetics : a road map membrane biology to biotechnology.
34.	15.02.2007	Dr. Will Stanley, CCMB. Hyderabad	Conformational flexibility in both receptor and cargo facilitate Peroxisomal protein import.
35.	23.02.2007	Prof. Miklos Nyerges, Univ. of Budapest, Hungary	Azomethine ylides; Cycloadditions and electrocyclisations.

MONTHLY COLLOQUIUM SEMINAR

No.	Date	Speaker	Title of Seminar
1.	14.06.2006	Prof. Yashwant D. Vankar, IIT, Kanpur	Synthesis of Newer Glycosidase Inhibitiors and Glycosamnio acids using Synthetic Carbohydrate Chemistry
2.	28.07.2006	Dr. Utpal Bhadra, CCMB	Small RNA's : Big Scope and Robust hope
3.	25.08.2006	Prof. Tapas Kr. Kundu, JNCASR, Bangalore	Chromatin Dynamics Links to Disease and Therapeutics
4.	19.10.2006	Prof. Debiprosad Nayak, University of California, USA	Host pathogenesis and vaccine development of influenza viruses
5.	21.12.2006	Prof. Anindya Dutta, Univ. of Virginia Health Science Centre, Charlottesville, VA, USA	MicroRNAs and short interfering RNAs for probing cell proliferation
6.	15.01.2007	Prof. Deepak Bastia, Dept. Of Biochemistry and Molecular Biology, USA	Control of replication termination and fork movement in the yeast genome by replication terminator proteins and intra-S phase checkpoint proteins


GOLDEN JUBILEE CELEBRATION
INTERNATIONAL SYMPOSIUM ON
CHEMICAL BIOLOGY
March 7-9, 2007
INDIAN INSTITUTE OF CHEMICAL BIOLOGY
PROF. M. VIJAYAN

Events 2006-2007

Date	Celebration
April 02, 2006	Golden Jubilee Celebration of IICB. Dr. H.S. Maiti, Director, CGCRI was the Chief Guest. Prof. A. Surolia, Director, National Institute of Immunology, New Delhi, delivered the Golden Jubilee Lecture. Prof. V.S. Chauhan, Director, International Centre for Genetic Engineering and Biotechnology, New Delhi, delivered the XIXth J.C. Ray Memorial Lecture. A popular lecture in Bengali was given by Dr. Chindra Mandal, Scientist, IICB.
August 15, 2006	Independence Day celebration at IICB
September 14, 2006	Hindi Day Celebration. Chief Guest was Prof. Prem Shankar Tripathi, Professor, Hindi Department, Surendra Nath College, Kolkata
September 19, 2006	Alzheimer's Day Celebration. A popular Lecture was delivered by Prof. J.J. Ghosh, Professor of Biochemistry, Calcutta University, on a topic entitled "Therapeutic Strategies for Neurodegenerative Disorder with Special Reference to Alzheimer's Disease". Another Lecture was given by Prof. Shyamal Das, Professor of Neurology, Bangur Institute of Neurology, Kolkata.
September 25, 2006	'OPEN HOUSE' programme for laboratory visit for outside students on the occasion of CSIR Foundation Day celebration, 2006
September 26, 2006	CSIR Foundation Day Celebration. Welcome address given by Prof. Siddhartha Ray, Director, IICB Inaugural Address delivered by Pof. S. Dattagupta, Director, IISER, Kolkata. Foundation Day Lecture was delivered by Dr. J. Gowrishankar, Director, CDFD, Hyderabad, on a topic entitled "R-Loops in transcription".
November 22–24, 2006	18th National Congress of Parasitology on 'Advances in Parasitology Research in Tropical Diseases'
December 28–29, 2006	CSIR Programme on Youth for Leadership in Science (CPYLS – 2006) was organized. Prof. Shymal Kanti Sanyal, Vice-chancellor, Jadavpur University as Guest-in-Chief. and Dr. H.S. Maity, Director, CGCRI delivered the introductory address.
December 29, 2006 – January 07, 2007	'Kolkata Neuroscience Workshop' – a total of 25 nos. of participants were attended from the various corner of India with 6 nos. from abroad.
January 08 – 09, 2007	Third International Symposium on "Neurodegeneration & Neuroprotection" and Society of Neurochemistry (India) Meeting.
January 26, 2007	Republic Day celebration at IICB
February 14 – 16, 2007	'International Symposium on Deconstructing Human Diseases : The Genomic Advantage' was organized during XXXII Annual Conference of Indian Society of Human Genetics.
March 07 – 09, 2007	IICB Golden Jubilee International Symposium. Prof. M. Vijayan, Honorary Professor, Indian Institute of Science, Bangalore, was the Guest-in-Chief.

Extramural Activities

INFECTIOUS DISEASES & IMMUNOLOGY

Invited Lectures

Dr. H. K. Majumder

Topic : DNA topoisomerase I of *Leishmania*: A fascinating story behind (NCP)
Venue : 18th National Congress of Parasitology at IICB.
Date : November 22-24, 2006

Topic : Gene fusion of bi-subunit topoisomerase I of Leishmania leads to an active monomeric enzyme with conserved type IB enzyme characteristics (BMB) -
Venue : International Conference on Chromosomes to Neurons at SINP
Date : January 12-14, 2007

Topic : Induction of apoptosis *Leishmania* by withaferin A in a steroidal lactone and a PKC inhibitor isolated from Withania somnifera.
Venue : National symposium on 21st Centenary Research & Biochemistry & Biophysics at Kalyani University.
Date : February 3, 2007

Topic : DNA topoisomerases targeted chemotherapy of *Leishmania*.
Venue : AICTE sponsored Refresher's course on "Drug Interactions and its Toxicity" of Jadavpur University at the Department of Pharmacy.
Date : February 12, 2007.

Topic : Programmed cell death in *Leishmania* induced by withaferin A, a steroidal lactone isolated from withania somnifera.
Venue : 75th AGM of the SBC (I) at JNU, New Delhi.
Date : December 8-11, 2006

Topic : Beautiful toposiomerases in *Leishmania*.
Venue : Indian Science Congress at Annamalai University.
Date : January 3-7, 2007

Topic : Biotechnology and IT.
Venue : Mallabhum University of Technology, Bishnupur, Bankura..
Date : February 17, 2007

Topic : Biotechnology for combating diseases.
Venue : Workshop for journalists on Biotechnology for food security and Human Health at Bose Institute, Kolkata.
Date : March 9-10, 2007

Topic : Molecular Biology of *Leishmania* Parasites in relation to drug development and diagnostics.
Venue : Haldia Institute of Technology.
Date : March 29, 2007

Dr. Pijush K. Das

Topic : Macrophage biology in relation to disease pathogenesis using leishmaniasis as the model macrophage disease.
Venue : Advanced Centre for Treatment Research and Education for Cancer (ACTREC), Kharghar, Navi Mumbai.
Date : August 22, 2006

Topic : Generation of a natural peptide with robust immunomodulatory activity for therapy against leishmaniasis.
Venue : 18th National Conference of Parasitology, IICB, Kolkata
Date : November 22-24, 2006

Topic : Towards generating a natural peptide with strong macrophage activating potential.
Venue : International conference, Integrative Physiology, Calcutta University, Kolkata
Date : January 8-10, 2007.

Topic : Cystatin induces nitric oxide generation and favourable T cell response through MAPK signaling and facilitates protective immunity in visceral leishmaniasis.
Venue : 33rd Indian Immunology Society Conference, AIIMS, New Delhi.
Date : January 28-31, 2007.

Dr. Chitra Mandal

Topic : Structural analysis of a bacterial 9-*O*acetylated glycoprotein found in patients suffering from visceral leishmaniasis in the Indian subcontinent.
Venue : Indian Institute of Science, Bangalore
Date : March 1-2, 2007

Topic : Anti-apoptotic role of *O*-acetylation of sialic acids, a clever way to escape immune survilance in childhood acute lymphoblastic leukemia.
Venue : AIIMS, New Delhi
Date : January 28 -31, 2007

Topic : Unraveling the mystry of *O*-acetylated sialic acids in Indian visceral leishmaniasis: A unique virulent marker of leishmania.
Venue : University of Delhi
Date : 26-29 November 2006

Topic : Visceral leishmaniasis and Pseudomonas aeruginosa coinfection : Discovering the hidden story.
Venue : Indian Institute of Chemical Biology, Kolkata
Date : November 22 - 24, 2006

Topic : 9-Oacetylated sialic acids: the way sugar speaks for the survival of cancer cells in childhood leukemia'
Venue : Annual Meeting of the Academy organized by Indian Academy of Sciences at Indore.
Date : November 10 to 12, 2006

Topic : Status of regulatory enzymes in the orchestration of cell surface sialylation of lymphoblasts in childhood Acute Lymphoblastic leukemia.
Venue : Guha Research Conference (GRC), in Mandala, Leh
Date : September 3-8, 2006

Topic : Mobilization of hematopoietic progenitor cells in childhood acute Lymphoblastic leukemia.
Venue : Heritage Institute of Technology, Kolkata
Date : April 5-6, 2006

Dr. Nahid Ali

Topic : Drug-induced differential polarization of the immune response in Indian kala-azar patients: Implications for the development of PKDL.
Venue : 75th Annual Meeting of SBC(I), JNU, New Delhi
Date : December 8-11, 2006

Topic : IL-10 and TGF-ß mediated susceptibility in kala-azar and post-kala-azar dermal leishmaniasis : The significance of amphotericin B in the context of *Leishmania donovani* infection in India.
Venue : 33rd Indian Immunology Society conference, AIIMS, New Delhi
Date : January 28-31, 2007

Dr. Rupak Bhadra

Topic : An overview of recent progress in microbial genomics
Venue : On inauguration of the PG-Microbiology Deptt, Midnapur College, Midnapur, West Bengal.
Date : September 14, 2006

Topic : CTX prophage array in the genome of *Vibrio cholerae* non-O1/non-O139
Venue : Presidency College, Kolkata.
Date : December 09, 2006

Topic : Bacterial pathophages and evolution of cholera pathogen
Venue : Department of Physiology, Serampur College, Serampur, West Bengal.
Date : March 10, 2007

Dr. Mridula Misra

Topic : Radiation Safety: An Overview
Venue : IICB
Date : August 31, 2006

Topic : Radiopharmaceuticals Design and Mechanism.
Venue : Jadavpur University
Date : September 16, 2006

Topic : Radiation Safety Guidelines : An Overview
Venue : NIO, Goa
Date : October 17, 2006

Topic : Radiopharmaceuticals Interaction and Toxicity.
Venue : Jadavpur University
Date : February 5, 2007

Chairing sessions

Dr. H. K. Majumder

Chaired a session in the XXXII Annual Conference of ISHG and International Symposium on Deconstructing Human Diseases: The Genomic advantage held at Science City, Kolkata February 14-16, 2007 sponsored by IICB.

Dr. Pijush K. Das

Chaired a session in XXXII Annual Conference of Indian Society of Human Genetics and International Symposium on Deconstructing Human Diseases: The Genomic Advantage. Science City, Kolkata, February 14-16, 2007.

Dr. Mridula Misra

Chaired a session for the 4th Annual Conference of Association of Nuclear Medicine Physicians of India (ANMPI) held on 13th - 15th October 2006 at Goa.

Chaired a session at 38th Annual Conference of "Society of Nuclear Medicine India" in collaboration with Tata Main Hospital on December 15, 2006.

Academic Performance: Teaching, examining and training

Dr. H. K. Majumder

Guest Professor, Department of Biophysics, Molecular Biology and Genetics, Calcutta University

Dr. Pijush K. Das

Guest Professor, M.Sc. (Biophys & Mol. Biol), M.Sc. (Biotechnology), M.Sc. (Microbiology), M.Sc. (Genetics) of Calcutta University, M.Tech (Biotech) of Jadavpur University and M.Tech (Biotech) of West Bengal University of Technical Education for teaching Biochemistry and Cell Biology.
Examiner in the M.Sc. (Biochemistry), M.Sc. (Biophysics & Molecular Biology), M.Sc.(Biotechnology), M.Sc. (Microbiology), M.Sc. (Genetics) at Calcutta University and M.Tech. (Biotech) at Jadavpur University

Dr. Chitra Mandal

Transfer of an antigen based diagnostic technology for diagnosis and monitoring of patients with visceral leishmaniasis to Zypher Biomedicals, Goa

Dr. Nahid Ali

Guided project of Mr. Dwijit Guha Sarkar for the partial fulfillment of M.Sc. (Biochemistry), 3rd semester curriculum, University of Calcutta, during May-August, 2006.

Guided project of Ms. Debjani Pal for the partial fulfillment of M.Sc. (Microbiology), 3rd semester curriculum,

University of Calcutta, during May-July, 2006.

Guided project of Mr. Rupam Kumar Bhunia for the partial fulfillment of M.Sc. (Applied Microbiology), Vellore Institute of Technology, during Nov 2006- May 2007.

Guided project of Mr. Govind Agarwal for the partial fulfillment of the requirements for the degree of B.Tech. (Bioinformatics), Vellore Institute of Technology, during Dec 2006- May 2007.

Dr. R. Chowdhury

Examiner in M.Sc. (Biochemistry), M.Sc. (Genetics), M.Sc. (Biotechnology) Calcutta University

Dr. Rupak Bhadra

Acted as an external examiner of Ph.D. viva voce examination of Jadavpur University, Kolkata

Dr. Tripti De

Examiner in M.Sc. Part II , Department of Biochemistry and Biophysics, University of Kalyani

Dr. Mridula Misra

Training: Organized "Training Programme and Workshop on Laboratory Safety (Chemical Safety, Radioactive Safety and Bio-Safety)" for the students and staff of IICB as convener on 31st August, 2007 in IICB.

Deputation Abroad

Dr. Chitra Mandal

Participation in a Special Programme on Diagnostics for Visceral Leishmaniasis sponsored by the UNICEF/UNDP/World Bank/WHO for Research and Training in Tropical Diseases (WHO/TDR). This consultation during 9-10 January 2006 in Nairobi, Kenya. And delivered a lecture on AN ANTIGEN BASED ERYTHROCYTE BINDING ASSAY FOR INDIAN VISCERAL LEISHMANIASIS

Conferences/Symposium/Workshops

Dr. Nahid Ali

Jt. Organizing Secretary of 18th National Congress of Parasitology, 2006 on Advances in Parasitology Research in Tropical Diseases, Nov 22-24, 2006, organized by IICB and ISP at Kolkata, India

Dr. Rupak Bhadra

One of the members of the Organizing Committee of XXXII Annual Conference of Indian Society of Human Genetics on and International Symposium Deconstructing Human Diseases: The Genomic Advantage (organized jointly by Indian Institute of Chemical Biology and Indian Society of Human Genetics) held during February 14-16, 2007, at Science City, Kolkata.

Papers/abstract presented in the conference

Dr. Chitra Mandal

Dutta, Avijit, Mandal, Debayan, Mondal, Nirup B., Banerjee, Sukdep, Sahu, Niranjan P., and Mandal, Chitra : Racemoside a, a steroidal saponin, from Asparagus racemosus induces programmed cell death in leishmania donovani promastigotes. Meeting on new trends in infectious disease research at Heidelberg, Germany, Nov 23-25, 2006.

Dr. Nahid Ali

Roychoudhury, J., Banerjee, A. and Ali, N. Therapeutic efficacy and mechanism of stearylamine-liposome based sodium antimony gluconate potency against antimonial-sensitive and resistant L. donovani infection. 18th National congress of Parasitology, IICB, Kolkata, November 22-24, 2006.

Banerjee, A., Roychoudhury, J. and Ali, N. Stearylamine-bearing cationic liposomes kill Leishmania parasites through surface exposed negatively charged phosphatidylserine. 18th National Congress of Parasitology, IICB, Kolkata, November 22-24, 2006.

Mazumder, S., Ravindran, R., Banerjee, A. and Ali, N. Non-coding plasmid DNA along with soluble leishmanial antigen entrapped into cationic liposomes elicit complete protection against experimental visceral leishmaniasis. 18th National Congress of Parasitology, IICB, Kolkata, November 22-24, 2006.

Bhowmick, S., Ravindran, R. and Ali N. Leishmanial antigens in liposomes promote protective immunity and provide immunotherapy against visceral leishmaniasis via polarized Th1 response. 18th National Congress of Parasitology, IICB, Kolkata, November 22-24, 2006.

Bhowmick, S., Palit, P. and Ali, N. A Leishmania donovani promastigote membrane antigen that stimulated a Th1 type cytokine profile in cured visceral leishmaniasis individuals induced protection in a murine model in association with cationic liposomes. 33rd Indian Immunology Society conference, AIIMS, New Delhi, January 28-31, 2007.

Roychoudhury, J. and Ali, N. Sub-optimal antimonials in stearylamine-bearing cationic liposome elicit substained cure against both antimonial-sensitive and -resistant strains of *Leishmania donovani* marked by increased antimony accumulation and favourable T cell responses. 33rd Indian Immunology Society conference, AIIMS, New Delhi, January 28-31, 2007.

Mondal, S., Saha, S., Rahman, M., Modak, D., Mallick, S., Goswami, R. P., Guha, S. K., Pramanik, N., Saha, B., and Ali, N. Characterization of immunosuppressive mechanism in Indian kala-azar and post kala-azar dermal leishmaniasis. 33rd Indian Immunology Society conference, AIIMS, New Delhi, January 28-31, 2007.

Mazumder, S., Ravindran, R., Banerjee, A. and Ali, N. Non-coding plasmid DNA co-entrapped with cationic liposomal soluble leishmanial antigens elicit almost complete protection against experimental visceral leishmaniasis. 33rd Indian Immunology Society conference, AIIMS, New Delhi, January 28-31, 2007.

Bhowmick, S. and Ali, N. Vaccination against kala-azar: A new invention. Bengal Science Congress, Jadavpur University, February 28-March 1, 2007.

Dr. Rupak Bhadra

Bhabatosh Das, Ritesh R. Pal and Rupak K. Bhadra on 'Construction and characterization of *Vibrio cholerae*

△relA △spoT double mutants' at the International Symposium on Chemical Biology' held during March 7-9, 2007 at Indian Institute of Chemical Biology, Kolkata, India.

Bhabatosh Das, Ritesh R. Pal and Rupak K. Bhadra.on 'Molecular characterization of *Vibrio cholerae* stringent response modulators' at the UGC Sponsored National Seminar on Biosensor held during March 24-25, 2007 at Post-Graduate Department of Raja N. L. Khan Women's College, Midnapur, West Bengal, India. Mr. Bhabatosh Das (SRF, ICMR) received best oral presentation award in this meeting.

Dr. Tripti De

Immunotherapeutic and immunoprophylactic potential of attenuated clonal population of Leishmania against lethal challenge with with virulent Leishmania donovani in Murine Model", selected for young scientist presentation in the 18th Nat. Cong. of Parasitol. Held at IICB, Nov 22-24,2006.

Identification, purification and partial characterization of 1,10 Phenanthroline sentsitive protease from Indian Strain of Kala-azar", Poster, although we wished her the greatest success in her new undertaking.

Protective efficacy of Leishmanial glycolipids against visceral leishmaniasis. Best Poster award at the 75th SBC meeting in Delhi, 2006

Dr. Mridula Misra

Susmita Chandra, Kakali De, Deblina Chatterjee, Mridula Misra "Global Cerebral Ischemia by two Vessel Occlusion: A potential Model for Nuclear Brain Imaging", Kolkata Neuroscience Meeting - 2007 and 3rd International Symposium on Neurodegeneration and Neuroprotection

CELL BIOLOGY & PHYSIOLOGY

Invited Lectures

Dr. Tuli Biswas

Topic : Oxidative denaturation of hemoglobin promotes premature hemolysis and contributes to the development of anemia in visceral leishmaniasis.
Venue : International Conference on Emerging Trends in Free Radical and Antioxidant Research, at Lonavala, India.
Date : January 8 - 11, 2007

Dr. Syed N. Kabir

Topic : Leptin: recent developments.
Venue : All India Congress of Obstetrics and Gynecology, Kolkata.
Date : 6-9 January, 2007

Topic : A randomized single-blind controlled trial of letrozole as a low-cost IVF protocol in women with poor ovarian response.
Venue : All India Congress of Obstetrics and Gynecology, Kolkata.
Date : 6-9 January, 2007

Dr. Arun Bandyopadhyay

Topic : Mechanism of glucocorticoid-induced cardiac malfunction in rat.
Venue : International Conference on Cardio-Pulmonary Regulation in Health and Disease: Molecular and Systemic Integration. Vallabhbhai Patel Chest Institute, University of Delhi.
Date : February 22-24, 2007

Topic : Altered expression of cardiac Ca^{2+} release channels genes in rat by dexamethasone.
Venue : International Conference on Frontier Researches in Integrative Physiology (ICFRIP), University of Calcutta.
Date : January 8-10, 2007

Topic : Inhibition of gene expression in hyperthyroid induced hypertrophied heart by free radicals.
Venue : 30thAll India Cell Biology Conference, Delhi University.
Date : February 2-4, 2007.

Dr. Sib Sankar Roy

Topic : Biochemical Mechanism of drug toxicity.
Venue : Jadavpur University.
Date : February 08, 2007.

Dr. K. P. Mohanakumar

Topic : Neurodegeneration and Neuroprotection.
Venue : NIDDK, NIH, Bethesda, USA.
Date : May 18, 2006.

Topic : Neurodegeneration and Neuroprotection in Parkinson's disease.
Venue : Spinal cord and Brain Injury Centre, University of Kentucky, Kentucky, USA.
Date : June 09, 2006.

Topic : The Ageing Mitochondria.
Venue : TRendys in Biochemistry, University of Hyderabad, Hyderabad.
Date : August 18, 2006.

Topic : Dying Neurons Die Hard.
Venue : Leh, J&K
Date : September 3-8, 2006.

Topic : Molecular Basis of Neurodegeneration and Neuroprotection in Neurodegenerative Diseases.
Venue : University Departmental Seminar: School of Life Sciences, Division of Animal Sciences, Department of Biochemistry, Hyderabad University.
Date : September 25, 2006.

Topic : Recent Advances in the etiology and therapeutics of Parkinson's disease.
Venue : Administrative Training College, Hyderabad University.
Date : October 05, 2006.

Topic : OH, NO, and apoptosis! The Up-, Mid-, and Down-stream events in dopaminergic neurodegeneration.
Venue : University Departmental Seminar: Department of Zoology, Division of Biochemistry, Banaras Hindu University, Varanasi.
Date : October 16, 2006.

Topic : Neuroendocrine regulation of neurodegeneration and neuroprotection with special reference to Parkinson's disease.
Venue : National Symposium on Trends & Techniques in Molecular Neuroendocrinology, University of Hyderabad.
Date : November 24, 2006.

Topic : Retrograde mode of degeneration of the dopaminergic neurons in Parkinson's disease.
Venue : 3rd NBRC International Conference, NBRC.
Date : December 13-15, 2006.

Topic : An assessment of mitochondrial dysfunction in Parkinson's disease.
Venue : Indo-US Workshop on Mitochondrial Research and Medicine, Centre for Cellular & Molecular Biology, Hyderabad
Date : January 22-24, 2007.

Topic : Neurobiology of Parkinson's disease.
Venue : National Symposium on "21st Century Research in Biochemistry & Biophysics" at Department of Biochemistry, Kalyani University.
Date : February 1-3, 2007.

Session Chairman

Dr. S. N. Kabir chaired a session in the Conference on Stress 2006, Ramakrishna Mission Seva Pratisthan, Kolkata, India, 10-11 June 2006.

Dr. S. N. Kabir chaired a session in the Conference on Advances in Reproductive Medicine, Kolkata, India on August 27, 2006.

Dr. S. N. Kabir: Panelist in a discussion on "Monitoring Glycemic Control in Diabetes", organized by ACADEMIA 2006, Kolkata, India,27-29 October 2006.

Academic Performance/Teaching

Dr. Tuli Biswas

Teaching of Physiology in the Coursework offered to PhD students of IICB, Kolkata.

Examiner of M.Sc. (Microbiology), Calcutta University.

External examiner of Ph. D. thesis and viva-voce of Calcutta University.

Supervised the project work of Mr. Sougata Roy for the submission of dissertation in connection to M.Sc. degree in Microbiology from Barrackpore Rastraguru Surendranath College, Barrackpore, West Bengal.

Dr Padma Das

Guided one student of Biju Patnaik Universitry of Technology for part fulfillment of Master of Pharmacy.

Dr. S. N. Kabir

Guest lecturer and Examiner, M.Sc, Physiology of Calcutta University and Vidyasagar University.

Guest lecturer, M.Sc, Physiology, Krishnath College, Murshidabad and Kalyani University.

External Examiner, M.Sc, Zoology (Endocrinology), Maulana Azad College, Kolkata.

Member of the board of Examiners in Physiology M. Sc. Part II, Presidency College, for Project and Seminar papers and viva-voce tests.

Dr. Sumantra Das

Delivered a course of lectures on Neurobiology as part of curriculum (Special paper) for second year M. Sc. Students of the Department of Biochemistry, Calcutta University.

External examiner & Question setter for the 1st Semester course for M. Sc. / Ph.D in neuroscience at the National Brain Research Centre, Manesar, Haryana.

Dr. Arun Bandyopadhyay

External examiner, Jadavpur University and Kalyani University.

Teaching Cell Biology in the course work offered to the PhD students of IICB

Dr. Sib Sankar Roy

UGC visiting teacher at Tripura University, Agartala to deliver a course to M. Sc. Life Science students.

Teaching Cell Biology in the course work offered to the PhD students of IICB

Examiner in the M. Sc. (Biotechemistry), M. Sc. (Microbiology) at Calcutta University, M. Sc. (Life Science) and M. Sc. (Biotechnology) at Visva Bharati University, M. Sc. (Life Science) at Tripura University, Agartala.

Deputations Abroad

Dr. K. P. Mohanakumar

Merina Varghese, SRF, CSIR participated in the International Workshop on Molecular Biology, Histopathology and Stem Cell Research in Neuroscience organized by the Neuroscience Society of Sri Lanka in collaboration with the Asian-Pacific Society for Neurochemistry at the University of Sri Jayewardenapura, Sri Lanka from December 14 to 18, 2006, availing a travel grant from the organizers.

Goutam Chandra, SRF, CSIR received Travel Award from Asia Pacific Society for Neurochemistry (APSN) for attending 7thbiennial meeting of Asia Pacific Society for Neurochemistry (APSN) held in Singapore from 2nd to 5thJuly 2006.

Goutam Chandra, SRF, CSIR received Travel Award from Japan Neuroscience Society (JNS) for attending 29th annual meeting of Japan Neuroscience Society (JNS) held in Kyoto, Japan from 19th to 21st July 2006.

Mritunjay Pandey, SRF, CSIR received Travel Award from Asia Pacific Society for Neurochemistry (APSN) for attending 7th biennial meeting of Asia Pacific Society for Neurochemistry (APSN) held in Singapore from 2nd to 5th July 2006.

Merina Varghese, SRF, CSIR received Travel Award from Asia Pacific Society for Neurochemistry (APSN) for attending 7th biennial meeting of Asia Pacific Society for Neurochemistry (APSN) held in Singapore from 2nd to 5th July 2006.

Reena Haobam, SRF, UGC received Travel Award from Asia Pacific Society for Neurochemistry (APSN) for attending 7th biennial meeting of Asia Pacific Society for Neurochemistry (APSN) held in Singapore from 2nd to 5th July 2006.

Sreetama Sen, SRF, UGC received Travel Award from Asia Pacific Society for Neurochemistry (APSN) for attending 7th biennial meeting of Asia Pacific Society for Neurochemistry (APSN) held in Singapore from 2nd to 5th July 2006.

Sreetma Sen, SRF, UGC was awarded the International Brain Research Organization-International Society for Neurochemistry (IBRO-ISN) fellowship for attending IBRO-ISN Neuroscience School and 7th biennial meeting of Asia Pacific Society for Neurochemistry (APSN) held in Singapore from 26th June to 5th July 2006.

Dr. Sumantra Das

Ishani Deb, SRF, UGC received Travel Award from Japan Neuroscience Society (JNS) for attending 29th annual meeting of Japan Neuroscience Society (JNS) held in Kyoto, Japan from 19th to 21st July 2006.

Mausam Ghosh, SRF, CSIR received Travel Award from International Brain Research Organization for attending the 1st Neuroscience Orientation Summer Program, at Neuroscience Research Center, Shaheed Beheshti University of Medical Sciences and Tarbiat Modares University, Tehran, Iran during September 2nd - September 21st, 2006.

Asmita Dasgupta, SRF, CSIR was awarded the International Brain Research Organization-International Society for Neurochemistry (IBRO-ISN) fellowship for attending IBRO-ISN Neuroscience School and 7th biennial meeting of Asia Pacific Society for Neurochemistry (APSN) held in Singapore from 26th June to 5th July 2006.

Conference Proceedings

Dutta Chowhury, K., Sen, G. and Biswas, T. Altered calcium homeostasis and membrane destabilization in erythrocytes of hamsters infected with *Leishmania donovani*. 18th National Congress of Parasitology, Kolkata, November 22 - 24, 2006.

Biswas, D., Sen, G., Giri, A. K. and Biswas, T. Pathological changes in erythrocytes in human population suffering from chronic arsenic exposure at different districts of West Bengal. 75th Annual Meeting of the Society of Biological Chemists (India), New Delhi, December 8 - 11, 2006.

Roy, D. N., Sen, G. and Biswas, T. Role of quercetin, a naturally occurring flavonoid in the prevention of copper induced toxicity in erythrocytes. XVIII Annual Conference of the Physiological Society of India, Kolkata, December 8 - 10, 2006.

Sen, G., Ray, M. and Biswas, T. Iron decompartmentalization in erythrocytes and heme catabolism associated with anemia during visceral leishmaniasis. International Conference on Emerging Trends in Free Radical and Antioxidant Research, Lonavala, January 8 - 11, 2007.

Saha Roy, S., Sen, G. and Biswas, T. Oxidative denaturation of hemoglobin promotes hemichrome binding to membrane, band 3 aggregation and erythrophagocytosis in visceral leishmaniasis. International Symposium on Chemical Biology, Kolkata, March 7 - 9, 2007.

Majumder, G. C., Saha, S., Das, K., Banerjee, S., Mandal, M., Maiti, A., Nath, D., Jaiswal, B. S., Paul, D., Mukherjee, A., Banerjee, S., Ghosh, A. K. and Dungdung, S. R. (2007) An Encounter with Sperm Flagellar Motility. In a national symposium on An Update on Reproductive Endocrinology: Novel and Applied Strategies on 26th -28th February, 2007 at Centre for Advanced study in Zoology, Zoology Department, Benaras Hindu University, Varanasi. p 5.

Das, K., Dungdung, S. R. and Majumder, G. C. Isolation of a sperm motility-inhibiting factor (SMIF) from goat caput sperm plasma membrane with antiagglutinin property. In IICB Golden Jubilee International Symposium on Chemical Biology on March 7-9, 2007 at IICB, Kolkata. India. p 82.

Saha, S., Dungdung, S. R., Paul, D., Mukherjee, A., Banerjee, S. and Majumder G. C. Novel Sperm Motility Regulators and A Novel Sperm Motility Analyzer. (Abstract): In IICB Golden Jubilee International Symposium on Chemical Biology on March 7-9, 2007 at Indian Institute of Chemical Biology, Kolkata. p. 79.

De, P., Ghose Roy, S. and Bandyopadhyay, A. Altered expression of cardiac Ca^{2+} release channels genes in rat by dexamethasone, International Conference on Frontier Researches in Integrative Physiology (ICFRIP), University of Calcutta, January 8-10, 2007.

Bandyopadhyay, A., Maity, S., De, K. and Ghosh, G. Inhibition of gene expression in hyperthyroid-induced hypertrophied heart by free radicals, 30th All India Cell Biology Conference and Symposium on "Molecules to Compartments: Cross-Talks and Networks", University of Delhi, Delhi, February 2-4, 2007.

Bandyopadhyay, A., Ghose Roy, S. and De, P. Mechanism of glucocorticoid-induced cardiac malfunction in rat, International Conference on Cardio-Pulmonary Regulation in Health and Disease: Molecular and Systemic Integration. Vallabhbhai Patel Chest Institute, University of Delhi, February 22-24, 2007.

Ghosh, P., Nandi, S. S., Saha, S. K. and Roy, S. S. Interaction of Pitx2 transcription factor with its target genes in ovary: a possible regulatory network in maintenance of ovarian structure and function. International symposium on Chemical Biology, held at IICB, Kolkata on March 7-9, 2007, page 78.

Chandra, G., Gangopadhyay, P. K. and Mohanakumar, K. P. Homocysteine and Parkinson's disease: Effects of acute intranigral administration on dopaminergic system. 29th Annual Meeting of the Japan Neuroscience Society (JNS), Kyoto, Japan, July 19-21, 2006. *Neurosci. Res., 55, S202, 2006.*

Chandra, G., Senthilkumar, K. S. Gangopadhyay, P. K. and Mohanakumar, K. P. Behavioral alterations and dopaminergic deficit following acute intranigral homocysteine administration in rodents: Relevance to Parkinson's disease. 7th Biennial meeting of the Asian Pacific Society for Neurochemistry, Singapore, 2-5 July, 2006. *J. Neurochem. 98, S(1), 116, 2006.*

Varghese, M. and Mohanakumar, K. P. Coenzyme Q10 increases mitochondrial complex-I and -IV activities of aged human subjects, but not Parkinson's disease patients: a cybrids study, 7th Biennial meeting of the Asian Pacific Society for Neurochemistry, Singapore, 2-5 July, 2006. *J. Neurochem. 98, S(1), 17, 2006.*
Pandey, M., Varghese, M., Sen, S., Sindhu, K. M., Mohanakumar, K. P. and Usha, R. Inhibition of complex-II of the mitochondrial electron transport chain leads to complex-I dysfunction in rats: relevance to Huntingotn's disease. 7th Biennial meeting of the Asian Pacific Society for Neurochemistry, Singapore, 2-5 July, 2006. *J. Neurochem. 98, S(1), 26, 2006.*

Sreetama, S., Banerjee, R., Pandey, M., Mohanakumar, K. P. and Usha, R. Proteasome inhibition: a major event in 3-nitropropionic acid-induced animal model of Huntington's disease, 7th Biennial meeting of the Asian Pacific Society for Neurochemistry, Singapore, 2-5 July, 2006. *J. Neurochem. 98, S(1), 26, 2006.*

Ghosh, M. and Das, S. Signaling through ß2-AR and its activators during thyroid hormone induced morphological differentiation of astrocytes. Quarterly Journal of the Iranian Society of Physiology and Pharmacology, 10 (Suppl-1): 29, 2006.

Ghosh, M. and Das, S. Downstream role of ?-adrenergic receptor subtype 2 during thyroid hormone induced morphological differentiation of astrocytes. 3rd International Symposium on Neurodegeneration and Neuroprotection, and Society for Neurochemistry (India) Meeting held in IICB, Kolkata during Jan 8-9, 2007.

Haobam, R., Sindhu, K. M., Saravanan, K. S., Varghese, M., Usha, R. and Mohanakumar, K. P. Nitric oxide, a mediator in rotenone-induced Parkinsonism in rats. 7th Biennial meeting of the Asian Pacific Society for Neurochemistry, Singapore, 2-5 July, 2006. *J Neurochem. 98, S(1), 115, 2006.*

Senthil Kumar, K. S, Saravanan, K. S., Sindhu, K. M. and Mohanakumar, K. P. Neuroprotection by L-deprenyl against oxidative stress-mediated dopaminergic neurodegeneration induced by rotenone in rats, *J Neurochem. 98, S(1), 100, 2006.*

Mohanakumar, K. P. Mitochondrial involvement in Parkinson's disease: Evidence from animal models, human brains and PD cybrids. *J Neurochem. 98, S(1), 115, 2006.*

Samanta, A., Gangopadhyay, P. K., Chandra, G., Haobam, R. and Mohanakumar, K. P. Serum acetylcholinesterase may be a marker of hepatic encephalopathy: neurological & biochemical investigations, 27th World Congress on Biomedical Laboratory Sciences, Seoul, Korea, Sept 15-19, 2006.

Haobam, R., Nair, R., Lenka, N. and Mohanakumar, K. P. Mouse embryonic stem cell derived dopaminergic neurons protects 6-hydroxydopamine-induced parkinsonism in rats', 3rd International Symposium on Neurodegeneration and Neuroprotection, and Society for Neurochemistry (India) Meeting held in IICB, Kolkata during Jan 8-9, 2007.

Samanta, A., Haobam, R., Chandra, G., Gangopadhyay, P. K. and Mohanakumar, K. P. Blood acetylcholinesterase may be a marker of hepatic encephalopathy: neurological & biochemical investigations. 3rd International Symposium on Neurodegeneration and Neuroprotection, and Society for Neurochemistry (India) Meeting held in IICB, Kolkata during Jan 8-9, 2007.

Sengupta, T., Pal, C., Nandi, D., Borah, A., Jaisankar, P. and Mohanakumar, K. P. Does an Ayurvedic preparation hold key to novel ingredients active against experimental Parkinson's disease? 3rd International Symposium on Neurodegeneration and Neuroprotection, and Society for Neurochemistry (India) Meeting held in IICB, Kolkata during Jan 8-9, 2007.

Gangopadhyay, P. K., Borah, A., Chandra, G. and Mohanakumar K. P. Homocysteine is a key factor for L-DOPA induced Parkinson's disease progression, 3rd International Symposium on Neurodegeneration and Neuroprotection, and Society for Neurochemistry (India) Meeting held in IICB, Kolkata during Jan 8-9, 2007
Mohanakumar, K. P. Neurodegeneration and neuroprotection: Parkinson's disease, 3rd International Symposium on Neurodegeneration and Neuroprotection, and Society for Neurochemistry (India) Meeting held in IICB, Kolkata during Jan 8-9, 2007.

Pandey, M., Varghese, M., Sindhu, K. M., Sreetama, S., Mohanakumar, K. P. and Usha, R. An inhibitor of mitochondrial succinate dehydrogenase, 3-nitropropionic acid causes multiple electron transport chain deficits in rat brain in an animal model of Huntington's disease 3rd International Symposium on Neurodegeneration and Neuroprotection, and Society for Neurochemistry (India) Meeting held in IICB, Kolkata during Jan 8-9, 2007.

Varghese, M. and Mohanakumar, K. P. Mitochondrial electron transport chain dysfunction in Parkinson's disease: an evaluation in human brain, platelets and cybrids, 3rd International Symposium on Neurodegeneration and Neuroprotection, and Society for Neurochemistry (India) Meeting held in IICB, Kolkata during Jan 8-9, 2007.

Borah, A., Sengupta, T. and Mohanakumar, K. P. Dopamine is formed in serotonergic neurons following long-term L-DOPA treatment, 3rd International Symposium on Neurodegeneration and Neuroprotection, and Society for Neurochemistry (India) Meeting held in IICB, Kolkata during Jan 8-9, 2007.

Dasgupta, A., Das, S. and Sarkar, P. K. Thyroid hormone stimulates γ- glutamyl transpeptidase as well as γ-glutamyl cysteine synthetase in astroglia cultures. In, Proceedings of International Conference on Free Radicals and Antioxidant in Health, Disease and Radiation and Vth Annual Conference of Society for Free Radical Research (SFRR)-India; Young Scientist Lecture, Abstract No. YS-5; Page-109, 2006.

Chandra, G., Borah, A., Gangopadhyay, P. K, Mohanakumar, K. P. Effects of long-term administration of L-DOPA on homocysteine levels, and its intranigral administration on dopaminergic neurons in rats 3rd International Symposium on Neurodegeneration and Neuroprotection, and Society for Neurochemistry (India) Meeting held in IICB, Kolkata during Jan 8-9, 2007

Navneet, A. K, Appukuttan, T. A., Pandey, M. and Mohanakumar, K. P. Taurine increases hydroxyl radical generation in the brain mitochondria, and fails to protect against MPTP-induced neurodegeneration, 3rd International Symposium on Neurodegeneration and Neuroprotection, and Society for Neurochemistry (India) Meeting held in IICB, Kolkata during Jan 8-9, 2007

Sen, S., Banerjee, R., Pandey, M., Mohanakumar, K. P. and Usha, R. Inhibition of glutamyl peptidase-like activity: a key event in 3-nitropropionic acid-induced animal model of Huntington's disease, 3rd International Symposium on Neurodegeneration and Neuroprotection, and Society for Neurochemistry (India) Meeting held in IICB, Kolkata during Jan 8-9, 2007

Bandyopadhyay S., Banerjee S., Pal D., Goswami S. K., Chakravarty B. N., Kabir S. N., The size of ovarian follicular quantum impacts the rate of follicular atresia" presented at Conference on Recent Advances and Challenges in Reproductive Health Research at New Delhil, India, February 19-21, 2007.

Chakraborty P., Goswami S. K., Chakravarty B. N., Kabir S. N.,"Altered trace mineral milieu may impact pathogenesis of polycystic ovarian disease" at Conference on Recent Advances and Challenges in Reproductive Health Research at New Delhil, India, February 19-21, 2007.

Chakraborti J., Goswami S. K., Chakravarty B. N., Kabir S. N., "PCO women with and without insulin resistance show differential leptin response to ovarian suppression and stimulation during controlled ovarian hyperstimulation" presented at Conference on Recent Advances and Challenges in Reproductive Health Research at New Delhil, India, February 19-21, 2007

Chakraborti J., Chatterjee R., Goswami S. K., Chakravarty B. N., Kabir S. N., Interactive relationship between leptin, body mass index and follicular response to in women with polycystic ovarian disease. presented at National Symposium on Cross-Talk between Zoology and Technology, November 16-17, 2006, University of North Bengal, Siliguri

Ray H. N., Sarkar S., Pal D., Gupta M., Pal B. C., Kabir S. N., "Spermicidal potential of two acylated triterpenoid bisglycoside saponins, isolated from the funicles of *Acacia auriculiformis"* presented at National Symposium on Cross-Talk between Zoology and Technology, November 16-17, 2006, University of North Bengal, Siliguri.

Das P.,"Experimental investigation on contragestative effects on statins" at the conference on Recent Advances and challenges in Reproductive Health Research at17th Annual Meeting of the Indian Society for the Study of Reproduction and Fertility (ISSRF) held 19th-21st February, 2007 at New Delhi

MOLECULAR & HUMAN GENETICS

Invited lectures

Dr Samit Adhya

Topic : "Restoration of respiratory function in cells containing a mitochondrial tRNA mutation causing Myclonic Epilepsy with Ragged Red Fibers by a parasite-derived tRNA Import Complex".
Venue : XXXII Annual Conference of Indian Society of Human Genetics, Calcutta.
Date : February 14-16, 2007.

Topic : "Genetic and proteomic analysis of the *Leishmania* mitochondrial tRNA import complex".
Venue : International Symposium on Chemical Biology, IICB.
Date : March 7-9, 2007.

Dr. Keya Chaudhuri

Topic : "Gene expression as a drug discovery too".
Venue : Dept. of Pharmaceutical Technology, Jadavpur University in AICTE Sponsored Refreshers' Course.
Date : July 21, 2006

Topic : "Application of transcription profiling in drug toxicity analysis".
Venue : Dept. of Pharmaceutical Technology, Jadavpur University in AICTE Sponsored Refreshers' Course.
Date : February 07, 2007

Topic : "Genetic variability in drug response and toxicity".
Venue : Dept. of Pharmaceutical Technology, Jadavpur University in AICTE Sponsored Refreshers' Course.
Date : February 07, 2007

Topic : "Host-*Vibrio cholerae* interaction: stimulation of IL-1β in human intestinal epithelial cells through TLR5 mediated pathway".
Venue : Jadavpur University, Sixth Annual Conference of Indian Association of Medical Microbiologists, West Bengal Chapter.
Date : February 25, 2007

Dr. Kunal Ray

Topic : "Role of genetics in the management of Wilson's Disease".
Venue : SN Pradhan Centre for Neurosciences (124th Birth Annivarsary of Dr. Bidhan Ch. Roy).
Date : July 3, 2006.

Topic : "Trends in Bioinformatics".
Venue : DOEACC Centre, Guwahati; Workshop on *Bioinformatics and its Future Prospects* organized by DOEACC Centre, Guwahati in association with Department of Botany, Guwahati University.
Date : July 9, 2006.

Topic : "Role of genetics in Human Diseases".
Venue : Lady Brabourne College, Kolkata (One day Seminar on "Role of genes and proteins in human health and diseases"l).
Date : July 27, 2006.

Topic : 'Gene Polymorphism".
Venue : Indian Institute of Chemical Biology (Kolkata Neuroscience Workshop; Dec. 29, 2006 - Jan. 7, 2007).
Date : December 29, 2006.

Topic : "Molecular Genetic Studies on Wilson's Disease in Indian Patients".
Venue : Annamalai University, Tamilnadu 94th Indian Science Congress.
Date : January 6, 2007.

Topic : "Molecular pathogenesis and genotype-phenotype correlation in Indian Wilson disease patients"
Venue : IICB, Kolkata [3rd International Symposium on "Neurodegeneration and Neuroprotection" & Society for Neurochemistry (India) Meeting; 8th & 9th January 2007]
Date : January 9, 2007

Dr. A.K. Giri

Invited lectures

Topic : "Assessment of health effects, genetic damage and genetic variants in the population exposed to arsenic through drinking water in West Bengal".
Venue : School of Earth, Atmospheric and Environmental Sciences, The University of Manchester, Williamson Bldg. Oxford Road, Manchester M13 9PL, United Kingdom.

Topic : "Polymorphism in the ERCC2 codon 751 is associated with arsenic-induced premalignant hyperkeratosis and significant chromosomal aberrations".
Venue : 3rd Asian Pacific Organization for Cancer Prevention General Assembly Conference (APOCP), Bangkok.
Date : November 3-5, 2006.

Topic : "Assessment of health effects and genetic variants in the arsenic exposed population in West Bengal"
Venue : XXXII Annual Conference of Environmental Mutagen Society of India (EMSI), Department of Environmental Sciences, PSE College of Arts and Science, Coimbatore, Tamil Nadu.
Date : January 10 - 12, 2007.

Topic : "Arsenic induced health effects: genomic approach to identify the arsenic susceptible individuals".
Venue : National Conference on "Genomics: Impact on Human Health", Department of Zoology, Osmania University, Hyderabad.
Date : February 2-3, 2007.

Topic : "Arsenic induced toxicity and health effects: genetic and genomic approaches to identify the arsenic suceptible individuals".
Venue : XXXII Annual Conference of Indian Society of Human Genetics & International Symposium on "Deconstructing Human Diseases: The Genomic Advantage" held at the Indian Institute of Chemical Biology, Kolkata

Date : February 14-16, 2007.
Topic : "Prolonged arsenic exposure induces toxicity, genetic damage and apoptosis via mitochondria-mediated pathway".
Venue : Indo-US Workshop on Mitochondria Related Research and Medicine, CCMB
Date : January 21-24, 2007

Dr. Susanta Roychaudhury

Topic : "*Host* susceptibility to *Helicobacter pylori* associated duodenal ulcer: functional insights in disease-associated IL1B polymorphisms".
Venue : Guha Research Conference, Leh.
Date : September 3-8, 2006

Topic : "Microsatellite in GI Malignancies".
Venue : GB Pant Hospital, Delhi.
Date : December 3, 2006

Topic : "Regulation of Gastrin Expression by *IL1B* Gene Promoter Polymorphism".
Venue : Transcription Assembly 2006, Kolkata.
Date : December 14-16 Feb ruary,2006.

Topic : "Host Susceptibilty to Helicobacter pylori mediated Gastroduodenal diseases: A genotype-Phenotype Correlation".
Venue : 32nd Annual Meeting of Indian Society of Human Genetics, Kolkata.
Date : February 14-16, 2007.

Topic : "Spindle assembly checkpoint defects in human cancer: overexpression of Cdc20 leads to aneuploidization in oral cancer".
Venue : Annual meeting of the Molcular Immunology Forum, Bangalore.
Date : March 1-2, 2007.

Session Chairman

Dr. Kunal Roy chaired a session on Genetics in the Annual Meeting of Indian Eye Research Group 2007 at L. V. Prasad Eye Institute, Hyderabad on July 30, 2006.

Dr. A.K. Giri chaired a Symposium Session at the XXXII Annual Conference of Environmental Mutagen Society of India (EMSI) which was held at the Department of Environmental Sciences, PSE College of Arts and Science, Coimbatore, Tamil Nadu from January 10 - 12, 2007.

Dr. A.K. Giri chaired a Session at the National Conference on "Genomics: Impact on Human Health" Which was held at the Department of Zoology, Osmania University, Hyderabad from Feb. 2-3, 2007.

Academic Performance / Teaching

Dr. Samit Adhya

Honorary lecturer and examiner of M.Sc. (Biophysics, Molecular Biology and Genetics), Calcutta University

Dr. Keya Chaudhuri

Examiner of the M.Sc. (Biotechnology), Calcutta University.

Reviewer of papers in FEMS Microbiology Letters, DNA and Cell Biology, BMC Microbiology, Journal of

Clinical Pathology and Indian Journal of Experimental Biology

Member of the Editorial Board of Research & Reviews in Biosciences published by Trade Science Inc., India

Dr. Kunal Ray

An honorary lecturer and examiner of the M. Sc. (Biotechnology), and M. Sc. (Genetics), Calcutta University. Teach Medical Genetics.

Delivered lectures in the UGC sponsored courses in Calcutta University

Member (External Expert) of a committee to perform function of Postgraduate Board for M.Sc. course in Genetics

Evaluated research proposals submitted to DST, DBT, CSIR etc. for funding.

Supervised six students (Debalina Banerjee, Allahabad University; N. Arti and Anindya Mukhopahdyay, Jiwaji University, Gwalior; Sobha George, Vellore Institute of Technology; Aninda Chatterjee and Aranyak Goswami, Calcutta University; and Sumit Kumar Dey, Jadavpur University) in the mandatory project work as part fulfillment of their various degrees like BTech, MSc and MTech.

Dr. A.K. Giri

Working as an Examiner at the Genetic Department, Centre of Advanced Study, Department of Botany, University of Calcutta.

Trained two students as summer training in laboratory.

Dr. Samir Dutta

M. Tech. Classes (Cal. Univ), M. Pharm (J. U.) dissertation examination etc.

Deputation abroad.

Dr. A. K. Giri visited University of California, Berkeley, USA from June 9-28, 2006 as an Exchange Faculty visit under the Fogarty International Training Program with the the University of California, Berkeley, USA and the Indian Institute of Chemical Biology, Kolkata.

Papers/Abstracts presented in the Conference

Suddhasil Mookherjee, Moulinath Acharya, Ashima Bhattacharjee, Kunal Ray, Silent mutation in *opticin* gene in POAG patient, Annual Meeting of Indian Eye Research Group' (July. 29 & 30, 2006) at the L. V. Prasad Eye Institute, Hyderabad. [Oral presentation].

Mahua Maulik, Moulinath Acharya, Suddhasil Mookherjee, Sanjay K.D. Thakur, Arun K Bandyopadhyay, and Kunal Ray, Primary role of *CYP1B1* in open angle glaucoma pathogenesis, 32nd Annual Meeting of the Indian Society of Human Genetics (ISHG) and International Symposium on "Deconstructing Human Diseases: The Genomic Advantage (14th-16th February, 2007) at Science City, Kolkata, Organized by IICB [Poster presentation]. Moulinath Acharya, Ashima Bhattacharjee, Suddhasil Mookherjee and Kunal Ray, Genetic and functional evidences of *CYP1B1* involvement in primary open angle glaucoma, 32nd Annual Meeting of the Indian Society of Human Genetics (ISHG) and International Symposium on "Deconstructing Human Diseases: The Genomic

Advantage (14th-16th February, 2007) at Science City, Kolkata, Organized by IICB [Oral presentation].

Ashima Bhattacharjee, Moulinath Acharya, Suddhasil Mookherjee, Deblina Banerjee, Sanjay Kumar Daulat Thakur, Arun K. Bandopadhyay, Abhijit Sen and Kunal Ray, L432V polymorphism in *CYP1B1* as a potential risk factor for POAG, 32nd Annual Meeting of the Indian Society of Human Genetics (ISHG) and International Symposium on "Deconstructing Human Diseases: The Genomic Advantage (14th-16th February, 2007) at Science City, Kolkata, Organized by IICB [Best poster presentation].

Suddhasil Mookherjee, Moulinath Acharya, Ashima Bhattacharjee, Arun K. Bandopadhyay, Sanjay Kumar Daulat Thakur, Abhijit Sen and Kunal Ray, L432V polymorphism in *CYP1B1* as a potential risk factor for POAG, Evaluation of *WDR36* as a candidate gene for Indian POAG patients, 32nd Annual Meeting of the Indian Society of Human Genetics (ISHG) and International Symposium on "Deconstructing Human Diseases: The Genomic Advantage (14th-16th February, 2007) at Science City, Kolkata, Organized by IICB [Poster presentation].

Atreyee Saha, Saibal Mukherjee, Mahua Maulik, Giriraj Ratan Chandak, and Kunal Ray, Evaluation of carrier detection efficiency of hemophilia A by DNA-based marker analysis: an Indian perspective, 32nd Annual Meeting of the Indian Society of Human Genetics (ISHG) and International Symposium on "Deconstructing Human Diseases: The Genomic Advantage (14th-16th February, 2007) at Science City, Kolkata, Organized by IICB [Poster presentation].

Poonam Nasipuri, Arnab Gupta, Ishita Chattopadhyay, Prasanta K. Gangopadhyay, Shyamal K. Das and Kunal Ray, Identification of a prevalent mutation in Indian Wilson disease patients, 32nd Annual Meeting of the Indian Society of Human Genetics (ISHG) and International Symposium on "Deconstructing Human Diseases: The Genomic Advantage (14th-16th February, 2007) at Science City, Kolkata, Organized by IICB [Poster presentation].

Ishita Chattopadhyay, Arnab Gupta, Poonam Nasipuri, Prasanta K. Gangopadhyay, Shyamal K. Das and Kunal Ray, Identification of a prevalent mutation in Indian Wilson disease patients, Evaluation of MURR1 gene as a modifier locus for Wilson's disease, 32nd Annual Meeting of the Indian Society of Human Genetics (ISHG) and International Symposium on "Deconstructing Human Diseases: The Genomic Advantage (14th-16th February, 2007) at Science City, Kolkata, Organized by IICB [Poster presentation].

Arindam Biswas, Kaumudee Bose, Pritha Ghosh, Ashoke K. Giri, Shyamal K. Das, Kunal Ray and Jharna Ray, Evaluation of GSTT1 and GSTM1 null genotypes with Parkinson's disease, 32nd Annual Meeting of the Indian Society of Human Genetics (ISHG) and International Symposium on "Deconstructing Human Diseases: The Genomic Advantage (14th-16th February, 2007) at Science City, Kolkata, Organized by IICB [Poster presentation].

Tufan Naiya, Arindam Biswas, Gautami Das, Kunal Ray, Shyamal Kumar Das, and Jharna Ray, Clinical and molecular genetic studies on Dystonia in Indian population, 32nd Annual Meeting of the Indian Society of Human Genetics (ISHG) and International Symposium on "Deconstructing Human Diseases: The Genomic Advantage (14th-16th February, 2007) at Science City, Kolkata, Organized by IICB [Poster presentation].

Moumita Chaki, Molecular genetic studies on pigmentation variation in human with special reference to Oculocutaneous albinism, 32nd Annual Meeting of the Indian Society of Human Genetics (ISHG) and International Symposium on "Deconstructing Human Diseases: The Genomic Advantage (14th-16th February, 2007) at Science City, Kolkata, Organized by IICB [Received Young Scientist Award].

Arunava Bandyopadhaya, Madhubanti Sarkar and Keya Chaudhuri 'Flagellin of Vibrio cholerae stimulates interleukin IL-1b expression through TLR5 mediated pathway at the symposium on ' Recent developments in modern biology' (May 19-21, 2006) organized by Society of Biological Chemists (India)-Kolkata at Digha, West Bengal.

De Chaudhuri, Sujata and Giri, A. K. (2007) Contribution of Purine Nucleoside Phosphorylase Polymorphisms in the Development of Arsenic Induced Skin Lesions. Paper presented at the XXXII Annual Conference of Environmental Mutagen Society of India (EMSI) which was held at the Department of Environmental Sciences, PSE College of Arts and Science, Coimbatore, Tamil Nadu from January 10 - 12, 2007.

Banerjee, Nilanjana and Giri, A. K. (2007) Induction of Apoptosis in the Lymphocytes of Arsenic Exposed Individuals in West Bengal, India. Poster presented at the XXXII Annual Conference of Environmental Mutagen Society of India (EMSI) which was held at the Department of Environmental Sciences, PSE College of Arts and Science, Coimbatore, Tamil Nadu from January 10 - 12, 2007.

Halder, Babli., Guha, Prasun., Mukhopadhyay, Sibabrata and Giri, A. K. (2007) Induction of Apoptosis and Inhibition of Cell Cycle Kinetics by Black Tea Polyphenols, Theaflavins and Thearubigins in Human Skin Cancer Cells. Poster presented at the XXXII Annual Conference of Environmental Mutagen Society of India (EMSI) which was held at the Department of Environmental Sciences, PSE College of Arts and Science, Coimbatore, Tamil Nadu from January 10 - 12, 2007.

Swati Bajaj, Sayan Mitra and Susanta Roychoudhury.'Polymorphism in p53 modulates the transcriptional regulation of asparagines synthetase gene promoter by both wild type and mutant p53' 2nd Bangalore Stem Cell Course and Workshop held at Jawahralal Nehru Centre for Advanced Scientific Research and National Center for Biological Sciences, TIFR, Bangalore, Nov 20-Dec 3, 2006 .

Swati Bajaj, Sayan Mitra,Chaitali Misra and Susanta Roychoudhury. 'Differential regulation of the asparagines synthetase gene promoter by the wild type and mutant p53 in the presence of codon 72 polymorphism' XXXIII Annual Conference of Indian Society of Human Genetics and International Symposium on Deconstructing Human Diseases: The Genomic Advantage held at Kolkata from Feb 14-16, 2007 .

Chaitali Misra, S. Mitra, S. Banerjee, A. Roy, A. Sengupta, C. K. Panda and S. Roychoudhury.'Studies on interplay between Human Papilloma Virus infection and p53 gene alterations in head and neck squamous cell carcinoma of a Indian patient population' Society of Biological Chemists (SBC) Seminar held at Digha. May, 2006.

Taraswi Banerjee, Somsubhra Nath, Gourish Mondal and Susanta Roychoudhury. ' Regulation of the expression of the Spindle Assembly Checkpoint Gene *CDC20* by p53 in response to DNA damage'. XXXIII Annual Conference of Indian Society of Human Genetics and International Symposium on Deconstructing Human Diseases: The Genomic Advantage, Kolkata, Feb 14-16, 2007.

Shiladitya Sengupta ."Tobacco intake leads to microsatellite instability in oral cancer cell lines by modulating the expression of MisMatch Repair pathway genes",.XXXII Annual Conference of Indian Society of Human Genetics & International Symposium on "Deconstructing Human Diseases: The Genome Advantage" Feb 14-16,2007, Kolkata.

Shiladitya Sengupta, Susmita Chakrabarti, Anup Roy, Chinmay K Panda and Susanta Roychoudhury. "Relation between promoter hypermethylation of hMLH1 and hMSH2 genes and microsatellite instability in HNSCC tumors", Annual Meeting of the Society of Biological Chemists; Kolkata Chapter 2006 (Digha).

Dipanjana Datta De, Meenakshi Chakravorty, Subhabrata Purakayastha, Abhijit Choudhury, and Susanta Roychoudhury "Interleukin 1beta (IL1B) as potential host susceptibility factor in Helicobacter pylori mediated duodenal ulcer in Eastern Indian Population" XXXIII Annual Conference of Indian Society of Human Genetics and International Symposium on Deconstructing Human Diseases: The Genomic Advantage, Kolkata Feb 14-16, 2007.

Sanhita Roy and Samir Kumar Dutta, Cloning, expression and bio-chemical characterization of a chymotrypsin/ trypsin inhibitor from a leguminous plant', '21st Century research in Biochemistry and Biophysics', Kalyani University, Feb 1-3, 2007.

DRUG DEVELOPMENT, DIAGNOSTICS & BIOTECHNOLOGY

Invited Lecture:

Dr. Snehasikta Swarnakar

Topic : Antioxidants block H_2O_2 mediated suppression of matrix metalloproteinase-2 expression and activity during healing of indomethacin-induced gastric ulcer
Venue : International conference on free radicals and antioxidants in health, disease and radiation, Kolkata.
Date : Jan 2006

Topic : Science and Environment
Venue : Golden Jubilee Celebration of Shyama Prasad Shikshayatan, Nadia, West Bengal.
Date : Jan 2006.

Topic : New dimension to prevent gastric ulcer
Venue : Science day celebration by Science Association of Bengal, Kolkata
Date : Feb 2006

Topic : Role of Metalloproteases in Endometriosis
Venue : One Day Symposium on Endometriosis, Kolkata
Date : June 2006

Topic : New pathways to prevent gastric ulcers: Emerging role of turmeric
Venue : Annual Conference of Association of Physiologists of Orissa, Bhubaneswar
Date : Nov 2006

Topic : Infection by *cag* negative *Helicobacter pylori* in C57BL/6 mice up regulates matrix metalloproteinase-9 expression and activity
Venue : Annual meeting of Society of Biological Chemists, New Delhi.
Date : Dec 2006.

Topic : A new function of curcumin and other antioxidants to prevent gastric ulcer by regulation of matrix metalloprotease-9 and 2
Venue : SFRR-ASIA 2007, Lonavala,
Date : Jan 2007.

Dr. Pratap K. Das

Topic : Gastric physiology, pathophysiology and therapeutic management - Role of metals
Venue : National Seminar on Interiors of Molecules from Ayurvedic metals and Mineral Preparations, Kolkata
Date : December 2-4, 2006

Topic : Revisiting Indian Biodiversity in Search of Newer Anti Peptic Ulcer Lead(s) - A Tale of Two Findings
Venue : 94th Indian Science Congress, Section of Biological Sciences (New Biology), Annamalai University, Annamalainagar
Date : January 3-7, 2007

Dr. Sharmila Chattopadhyay

Topic : Genetic improvement of traditionally used Indian medicinal plants
Venue : National Symposium on Plant Biotechnology & Annual Conference of PTCA, FRI, Dehradun
Date : 12-14th October 2006.

Topic : Tissue specific overexpression of gene encoding GSH biosynthetic pathway's enzyme in transgenic *Phyllanthus amarus*.
Venue : 30th All India Cell Biology Conference, New Delhi
Date : 2-4 Feb. 2007

Session Chairman

Dr. Snehasikta Swarnakar chaired a session at Annual Conference of Association of Physiologists of Orissa, Bhubneswar, India. Nov 2006

Academic Performance/Teaching

Dr. Tarun Kumar Dhar

Reviewer of papers to be published in Analytica Chimica Acta
Acted as a Judge of the Poster session at Heritage Institute of Technology, Kolkata.

Dr. Pratap K. Das

Visiting Faculty in the Department of Bioscience & Engineering, Jadavpur University - Teaching Biochemistry to Students of M. Tech. in Biomedical Engineering.

Dr. Snehasikta Swarnakar

Invited reviewer for the Journal of Cellular Physiology, USA

Invited reviewer of the Journal GUT, UK, 2006

Invited reviewer of Scan. J. Gastroenterol, Netherland, 2007

M.Sc examiner of Dept. of Microbiology, Calcutta University.

Visiting Faculty of M.Sc. course in Environmental Sc., Calcutta University
Teaching advance Ph.D. Course work at IICB & Ph.D. programme in Special Centre for Molecular Medicine at JNU, New Delhi.

Question setter of Biology section of JBNST Examination

Board member of SFRR-ASIA

Dr (Mrs) Aparna Gomes

Reviewer of Indian Journal of Physiology, Phytotherapy Research, Journal of medicinal plant research

Dr. Sharmila Chattopadhyay

Acted as reviewer of a project proposal entitled "Evaluation of anti-leishmanial phytochemical constituents of Aloe vera leaf exudates" for Senior Research Fellowship of ICMR, New Delhi.

Acted as external examiner of M.Sc (Biotech), Birsa Agricultural University, Ranchi, Jharkhand for Thesis evaluation and to conduct vive-voce and oral comprehensive examination.

Evaluated a Manuscript entitled "Antiulcerogenic and antioxidant effects of Coccinia grandis" in the Journal Natural Product Radiance, NISCAIR, New Delhi.

Interacted with M.Sc (Biotechnology) students of BIRSA Agriculture Univiversity on 18th December 2006.

Dr. (Mrs.) Suman Khowala

Ph. D. examiner of Biochemistry Department, Anna Malai University, Department of Genetics, Madurai Kamraj University.

Reviewer of Biotechnology Progress, a journal of American Chemical Society & Inst of Chemical Engineers, USA.

Reviewer of Electronic journal of Biotechnology

Dr. Nirmalendu Das

Nominated as a member of Academic Advisory Council at St Xavier College, Kolkata, Biotechnology And Microbiology Department 2006-07.

Paper/Abstract presented in the Conference

Saha D, Acharya D, Roy D and Dhar TK, 'Filtration-based tyramide amplification technique: A new simple approach for rapid detection of aflatoxinB1' presented at the 14th West Bengal Science & Technology Congress at Jadavpur University, Kolkata, Feburary 28th to 1st March 2007.

Saha D, Acharya D, Roy D, Srestha D and Dhar TK, 'Development of a rapid analytical method for the simultaneous determination of aflatoxin B1 and ochratoxin A in chilies by simple flow-through enzyme immunoassay' presented at the International Symposium on Chemical Biology at IICB, Kolkata, March 7-9, 2007.

Gomes, A., Das Gupta, S. and Vedasiromoni, J. R. 'Antileukemic activity of Indian Black Scorpion *(Heterometrus bengalensis)* venom against human leukemic U937 and K562 cells' presented at the conference of International Society of Toxinology, held at Glasgow, Scotland, July 23-28, 2006.

Roy, S., Mallick, S., Besra,S. E., Banerjee, B., Mitra, S. and Vedasiromoni, J. R. 'Anti-inflammatory activity of aqueous methanolic extract of *Swietenia mahagoni leaves'*, presented at XVIII Annual conference of Physiological Society of India, held at Presidency College, Kolkata. December 8-10,2006.

Besra,S., Roy, S., Nandi, D. K., Tripathi, G., Mitra, S., Banerjee, B. and Vedasiromoni, J. R. 'Pharmacological studies with aqueous methanolic leaf extract of *Swietenia mahagoni* with special reference to anti-inflammatory and anti-cancer activity' presented at XXXIX Annual conference of the Indian Pharmacological Society, held at Jaipur, December 21-23, 2006.
Roy, S., Besra, S. E., Mitra, S., Tripathi, G., Banerjee, B. and Vedasiromoni, J. R. 'Anti-leukemic activity of aqueous methanolic extract of *Litchi chinensis* leaves' presented at XXXIX Annual conference of the Indian Pharmacological Society, held at Jaipur. December 21-23, 2006.

Nandi, D. K., Soma Roy, Besra, S. E., Tripathi, G., Giri, V. S., Jaisankar, P. and Vedasiromoni, J. R. 'Extraction, fractionation and anti-inflammatory and anti-leukemic studies with the leaves of *Wattakaka volublis*' presented at XXXIX Annual conference of the Indian Pharmacological Society, , held at Jaipur. December 21-23, 2006.

Das Gupta, S., Gomes, A. and Vedasiromoni, J. R. 'Antineoplastic action of Indian Black Scorpion Venom (*Heterometrus bengalensis* Koch) against murine solid tumor model' presented at XXXIX Annual Conference of Indian Pharmacological Society, held at Jaipur . December 21-23, 2006.

Anindita, D., Vedasiromoni, J.R. and Gomes A. 'Chemical characterization, pharmacological and subchronic toxicity studies of antileukemic compound (NK-31) identified from the Indian monocled cobra (*Naja kaouthia*) venom' presented at 3rd International Symposium on "Neurodegeneration and Neuroprotection" held at IICB Kolkata, 2007.

Ghosh, S., Besra, S. E., Roy, K., Vedasiromoni, J. R. and Gupta, J. K. 'Anti-inflammatory effect of methanolic extract of *Swietenia mahagoni* Jacq. (Meliaceae) seeds' presented at XVII Annual state conference of Indian Pharmacological Society,West Bengal branch, held at Medical College, kolkata. 24th February, 2007.

Ghosh, P., Besra, S. E., Mitra, S. and Vedasiromoni, J. R. 'Cytotoxic and apoptogenic effect of tea root extract on Ehrlich's ascites carcinoma in mice along with significant antioxidant potential' presented at XVII Annual state conference of Indian Pharmacological Society, West Bengal branch, held at Medical College, Kolkata. 24th February 2007.

Debnath, A., Vedasiromoni, J. R. and Gomes, A. 'Indian cobra venom potently inhibits leukemic cell growth through apoptosis and cell cycle arrest' presented at International Symposium on Chemical Biology, held at IICB, Kolkata 2007.

Malakar, D. and Ghosh, A. K. 'A protective role of S-adenosyl-L-methionine against hydrochloric acid stress in *Saccharomyces cerevisiae'* presented at 29th AICBC meeting in ITRC, Lucknow, January 17 - 20, 2006.

Ganguly, K., Kundu, P., Banerjee, A. and Swarnakar, S. A novel role of melatonin and other antioxidants to block indomethacin-induced gastric ulcer through upregulation of matrix metalloprotease-2 activity and expression. (2006). Proceeding of the International Symposium on Teaching, Research, and Exploration in Biochemistry, Kolkata.

Kundu, P., Mukhopadhyay, A. K., Patra, R., Banerjee, A., Berg, D.E. and Swarnakar, S. Infection by cag negative *Helicobacter pylori* strain in C57/BL6 mice upregulates matrix metalloproteinase-9 expression and activity (2006) Proceeding of the International Symposium on Teaching, Research, and Exploration in Biochemistry: Kolkata.

Paul, S., Mishra, A., Bhattacharya, P., Das Mahapatra, P., Swarnakar, S. 'Role of metalloproteinases in endometriosis' presented at 21st Annual conference of All India Coordinating Committee Royal College Of Obstetricians and Gynaecologists (AICC RCOG), Science City, Kolkata, 2006.

Singh, L.P., Kundu, P., Ganguly, K., Mishra, A. and Swarnakar, S. 'Antioxidant role of famotidine in inhibition of matrix metalloproteinase-9 upregulation during protection of ethanol-induced gastric ulcer' presented at International conference on frontier researches in integrative physiology, Kolkata, 2007.

Sharma, A.V., Ganguly, K., Paul, S. and Swarnakar, S. 'Curcumin promotes angiogenesis by upregulation of matrix metalloproteinase-2 via vascular endothelial growth factor during healing of gastric ulcer' presented at International conference on frontier researches in integrative physiology, Kolkata, 2007.

Ghanta, S. and Chattopadhyay, S. 'Genetic improvement of traditionally used Indian medicinal plants' presented at 14th West Bengal State Science & Technology Congress Jadavpur University, 28th February to 1st March 2007.

Poddar, A. and Chattopadhyay, S. 'Potential Indian Medicinal Plants to combat kala-azar' presented at 14th West Bengal State Science & Technology Congress, Jadavpur University, 28th February to 1st March 2007.

Goswami, S. and Das, P.K. (2006). 'Detection and quantification of ppb level K^+ in biological samples in the presence of high Na^+ by ion chromatographic method', presented at 19th Annual International Ion Chromatographic Symposium. Pittsburgh, Pennsylvania, USA, September 24-27, 2006.

Das, P. K., Goswami, S, and Annalakshmi, C. 'Gastric physiology, pathophysiology and therapeutic management: role of metals' presented at National seminar on Interior of Molecules from *Ayurvedic* Metal and Mineral Preparations. Science City, Kolkata, December 2-4, 2006.

Das P. K., Goswami, S., Annalakshmi, C. and Kar, S.K. 'Revisiting Indian biodiversity in search of newer anti peptic ulcer lead(s) 3/4 A Tale of Two Findings', presented at 94th Indian Science Congress, Section of Biological Sciences (New Biology), Annamalai University, Annamalainagar. January 3-7, 2007.

Goswami, S., Annalakshmi, C., Banerjee, S., Sahu, N. P., Achari, B. and Das, P. K. 'Bioassay guided isolation of a potent anti gastric ulcer lead molecule from a plant flower', presented at International Symposium on Chemical Biology. IICB, Kolkata, March 7-9, 2007.

CHEMISTRY

Session Chairman

Dr. A. K. Sen, Jr. chaired a Technical Session at the XXI Carbohydrate Conference, University of Delhi, Delhi, 26-29 November, 2006.

Dr. P. Jaisankar chaired a Technical Session at Two Day National Seminar on "Clinical Research - Practice & Perspective" organized by Jadavpur University, Calcutta, 30th September to 1st October 2005.

Dr. P. Jaisankar chaired a Technical Session at Two Day National symposium on "Application of Catalysis in Day To Day Life" organized by A. W. College, Ottur, Pune, 24-25 March, 2006.

Academic Performance / Teaching

Dr. V. S. Giri

Served as Ph. D. Examiner of Jadavpur University. and Pune University.

External examiner for MSc (Envir. Sc.), Calcutta University.

Dr. Partha Chattopadhyay

Honorary guest faculty member for Post Graduate Teaching, Department of Chemistry, Scottish Church College, Kolkata.

Acting as a Reviewer of *Journal of Organic Chemistry*, American Chemical Society, 2007 and *Tetrahedron Letters* (Elsevier Science Ltd.) , 2007.

Dr. G. Suresh Kumar

Acting as a member of the editorial board of the *International Journal of Physical sciences*, Academic Journals and also as a reviewer for the African Journal of Biochemistry Research and International Journal of Biological Macromolecules (Elsevier)

Mr. Prateek Pandya, Research Scholar, Dayalbagh Educational Institute, Agra was given training in characterizing drug-DNA complexes by various physico-chemical techniques for three weeks during 11.9.06 to 21.9.06 and 13.02.07 to 21.02.07.

Dr. R.C. Yadav

Delivered a series of lectures on "Instrumental Techniques in Chemical Analysis" for the PG Diploma Course of Department of Adult Continuing Education & Extension, Jadavpur University.

Dr. S. Mukhopadhyay

Honorary guest faculty member for Post Graduate Teaching, Department of Organic Chemistry, Calcutta University.

Examinar of Ph. D. Thesis, Osmania University and Viswabharati

Dr. A. K. Sen, Jr.

Guest teacher at the B.Tech. course work, Raja Bazar Science College, Calcutta University.

Ph.D. thesis examiner Burdwan University, Jadavpur University and CFTRI, Mysore.

Editor of the 'Carbohydrate News Letter' a biannual publication of the Association of Carbohydrate Chemists & Technologists (India).

Dr. A. K. Banerjee

Acting as a Reviewer of *Organic Letters* and *Journal of Organic Chemistry*, American Chemical Society.

Acting as a member of the Board of Examiners in Chemistry for M. Sc. Part-II, Calcutta University and examiner in M.Sc Chemistry, Jadavpur University

Dr. Chinmay Chowdhury

Acting as a Reviewer of *Organic Letters* and *Journal of Organic Chemistry*, American Chemical Society.

Papers/Abstracts presented during Seminar/Symposium

Dr. P. Jaisankar

Nandi, D., Roy, S., Besra, S.E., Tripathi, G., Giri, V.S., Jaisankar, P.,Vedasironmoni, J.R. Extraction, fractination and anti-inflammatory, anti-leukemic studies with the leaves of Wattakaka volubilis. 39th Annual Conference, Indian Pharmacological Society, Jaipur, December 21-23, 2006.

Churala Pal, Sumit Dey, Amit Roy, Prasun K. Pradhan, Arumugam Meyyappan, Shila E. Besra, Venkatachalam S. Giri, Hemanta K. Majumader, J. Rajan Vedasiromoni and Parasuraman Jaisankar '.3,3(- Diindolylmethane (DIM) and itsderivatives ::Promi-sing agents as anti-cancer, anti-leishmanial and plant growth promoters "International Symposium on chemical Biology" organized by Indian Institute of Chemical Biology, Jadavpur, Kolkata. March 7-9, 2007.

Dr. Partha Chattopadhyay

Neogi, A., Das Adhkari, N., Chattopadhyay, P. Sequential N-benzylation and Pd-mediated Intramolecular Aryl amination on Furanose Derivatives: Construction of Enantiopure benzofused Dibenzoheterocycles: at the *International Symposium on Current Perspectives in Organic Chemistry*, Dept. of Organic Chemistry, Indian Association for the Cultivation of Science, Kolkata. India, December 7-9, 2006.

Dr. A. K. Sen, Jr.

Koushik Mazumder and Asish K Sen Studies on the O-Antigenic Polysaccharide Isolated from the Lipopolysaccharide of *Vibrio parahaemolyticus* O3K6, at the XXI Carbohydrate Conference, University of Delhi, Delhi, 26-29 November, 2006.

Koushik Mazumder, Gora Das and Asish K Sen Synthesis of the Terminal Disaccharide and its Protein Conjugate fo the O-Antigenic Polysaccharide of *Vibrio cholerae* O-37, at the XXI Carbohydrate Conference, University of Delhi, Delhi, 26-29 November, 2006.

Koushik Mazumder and Asish K Sen, Structural Studies on the O-Antigenic Polysaccharide Isolated from the Lipopolysaccharide of *Vibrio parahaemolyticus* O3K6, at the International Symposium on Chemical Biology, IICB, Kolkata, March 7-9, 2007

Dr. G. Suresh Kumar

Bhadra, K., Maiti, M. and Suresh Kumar, G. Interaction of palmatine with polymorphic DNA conformations: Spectroscopic, viscometric, competitive dialysis and thermodynamic studies. Fifth East Asian Biophysics Symposium and Forty-Fourth Annual Meeting of the Biophysical Society of Japan, Okinawa, Japan, November 12-16, 2006..

Sinha, R. and Suresh Kumar, G. RNA Interaction of DNA binding drugs to RNA structures: Binding of intercalator quinacrine versus groove binder DAPI to poly(rC).poly(rG). National Symposium on Current Trends in Chemistry, Kalyani, January 30-31, 2007.

Giri, P. and Suresh Kumar, G. Interaction of plant alkaloid palmatine with polyadenylic acid structures: spectroscopic and thermodynamic studies, National Conference on Photoscience, Kolkata, January 31, 2007.

Islam, Md. M., Sinha, R. and Suresh Kumar, G. RNA binding small molecules: studies on t-RNA binding by cytotoxic plant alkaloids berberine, palmatine and the comparison to ethidium, National Symposium on Biophysics; Trends in Biomedical Research, New Delhi, February 13-15, 2007

Sinha, R., Hossain M. and Suresh Kumar, G. RNA targeting by DNA binding drugs; Binding of quinacrine and DAPI to poly((rC).poly(rG) structures, National Symposium on Biophysics; Trends in Biomedical Research, New Delhi, February 13-15, 2007.

Sinha, R., Hossain M. and Suresh Kumar, G. RNA targeted drug Design: Studies on the binding of quinacrine and DAPI to poly(rC).poly(rG). International Symposium on Chemical Biology, Kolkata, March 7-9, 2007.

Islam, Md. M., Sinha R. and Suresh Kumar, G. RNA binding by protoberberine alkaloids; Studies on t-RNA binding of cytotoxic plant alkaloids berberine and palmatine. International Symposium on Chemical Biology, Kolkata, March 7-9, 2007.

Giri, P. and Suresh Kumar, G. RNA targeted drug design: Specific binding and self structure induction in polyadenylic acid by the alkaloid sanguinarine. International Symposium on Chemical Biology, Kolkata, March 7-9, 2007

Hossain, M., Giri, P. and Suresh Kumar, G. Structural features, stability and energetics of polymorphic DNA interaction with ethidium, methylene blue, quinacrine and sanguinarine. International Symposium on Chemical Biology, Kolkata, March 7-9, 2007.

STRUCTURAL BIOLOGY & BIOINFORMATICS

Invited Lectures

Prof. Siddhartha Roy

Venue : Niels Bhor Institute, University of Copenhagen; Denmark.
Date : 2nd to 7th May 2006.

Dr. M. C. Bagchi

Venue : National Institute of Chemistry, Slovenia.
Topic : Mathematical Modelling in Anti-tuberculosis Drug Design.
Date : 20th April, 2006.

Venue : Department of Pharmaceutical Technology, Jadavpur University (QIP Programme)
Topic : Calculated Molecular descriptors and Anti-tuberculosis Drug Design.
Date : 11th July, 2006

Dr. Chhabinath Mandal

Venue : "Second Medical Development Congress" organized by ICMR, Assocham House, 47, Prithvi Raj Road, New Delhi-11.
Topic : "Molecular Modeling and Drug Design - Their application in proteomics.
Date : 8-9th Sept. 2006.

Venue : National Symposium on Medicinal Plants: Role of Biotechnology and Bioinformatics, Birla Institute of Technology (BIT), Mesra, Ranchi.
Topic : Molecular Modeling and Drug Design - Emerging Fields of Biotechnology and Bioinformatics.
Date : August 3-5, 2006

Venue : SGI Technology Summit 2006, The Park Hotel, Kolkata.
Topic : User Perspective on Molecular modeling and drug design.
Date : May 12, 2006.

Dr. Chitra Dutta

Topic : Bioinformatics : Current State of Art
Venue : National Seminar on "Recent Trends in Information Systems", Jadavpur University
Date : July 14, 2006

Topic : Selection-Mutation Balance in Genome Evolution
Venue : Indian Association for Cultivation of Sciences, Kolkata
Date : August 4, 2006

Topic : Genome Projects & Beyond
Venue : Lady Brabourne College
Date : November 23, 2006

Dr Debasish Bhattacharyya

Topic : 'Regulation of catalysis in epimerase from yeast'
Venue : IMTECH, Chandigarh
Date : 15 Jan 2007

Dr. Nanda Ghoshal

Topic : Structure based drug design and lead optimization when there is no receptor crystal structure.
Venue : BIT'4th Annual Congress of International Drug Discovery Science & Technology, Dalian and Xian, China
Date : May 25-June 2, 2006

Topic : Structure Based Drug Design and Lead Optimization using RI & RD QSAR Studies.
Venue : Biopolymers in Drug Design and Drug Delivery, Department of Chemical Technology, University of Calcutta.
Date : Nov. 10-11, 2006

Dr. Krishnananda Chattopadhyay

Topic : Fluorescence correlation spectroscopy and protein folding in the microsecond time scale.
Venue : Workshop on structure and dynamics of biomolecules, S. N. Bose National Centre for Basic Sciences, Kolkata 700098
Date : Dec03-08, 2007

Dr. Subrata Adak

Topic : Evolutional design of a hyperactive mutant of Leishmania major ascorbate peroxidase
Venue : 75th Annual meeting of Society of Biological Chemists (India), Jawaharlal Nehru University, New Delhi.
Date : December 8-11, 2006

Session Chairman

Dr. Chitra Dutta

Chaired a sesion on "Bioinformatics" of "International Conference on Chromosomes to Neurons", held at Saha Institute of Nuclear Physics, Kolkata during January 12-14, 2007

Academic Performance/Teaching

Dr. M. C. Bagchi

Served as a reviewer for QSAR and Combinatorial Science, Chem Med Chem and Indian Journal of Biochemistry and Biophysics.

Acted as a coordinator of Statistics course for Ph.D. students of IICB

Evaluated proposal for funding for the International Symposium on Filament Protein as requested by Indo-US Science & Technology Forum.

Dr. Chitra Dutta

Guest Lecturer and Examiner, M. Sc. (Genetics), Calcutta University.

Paper-setter and Examiner, M. Sc. (biotechnology), University of Burdwan.

Examiner (Grand-viva): Advanced diploma in Bioinformatics, Calcutta University.

Moderator and Examiner : B. Tech (Biotechnology) and M. Tech. (Bioinformatics), West Bengal University of Technology

Dr Debasish Bhattacharyya

Served as a guest lecturer at the Department of Bio-Technology, Jadavpur University, Calcutta (M.Sc. Bio-Tech.).

Served as a guest lecturer at the Department of Zoology, Bethune College, University of Calcutta (M.Sc. Part I, Proteins and Enzymology).

Dr. Nanda Ghoshal

Acted as Examiner for M.Pharm. final (thesis and corresponding oral) examination, J.U. (of two candidates), held on June 9, 2006 at Pharmaceutical Technology Div., J.U.

Taken classes as a faculty in the training programme "Computer Course for Biologists" for Research Scholars, organized by IICB on the following topics during July-September, 2006:
Introduction to Molecular Modelling
Molecular Modelling in relation to Drug Designing.

Reviewer for manuscripts to be published in Bioorganic & Med. Chem. Letters.

Delivered Invited Lectures in the Department of Biotechnology, Visva - Bharati, Shantineketan to M.Sc. Biotechnology students and interacted with them (January 14, 2007).
Lecture Topics: 1. "Computer Aided Drug Design - QSAR Approach " 2. "RI and RD QSAR Studies for Drug Designing"

Invited to join the "Board of Studies Meeting to consider a course of M.Tech in Bioinformatics" As External Expert at Bengal Engineering & Science University, Shibpur, held on Feb. 23, 2007 . Actively participated in the meeting.

Evaluated Proposal for Indo-US Workshop, Submitted to Indo-US Science Technology Forum (March, 2007).

Krishnananda Chattopadhyay

Fluorescence Spectroscopy, Department of Biotechnology, Kolkata University

Dr. Saumen Datta

X-ray crystallographic courses (Basic and Advanced) in Ph. D course work at IICB

Dr. Subrata Adak

Examiner in M.Sc (Microbiology) and M. Sc (Genetics) of Calcutta University.

Examiner in B. Tech. (Biotechnology) of Haldia Institute of Technology.

Examiner in M.Sc (Biotechnology) of Uttar Banga University

Deputation Abroad

Dr. M. C. Bagchi

Worked as a visiting scientist in National Institute of Chemistry, Ljubljana, Slovenia during 16 April-15 May, 2006

Papers/Abstract Presented in the Conference

Nandi S., Bagchi M. C. & Vracko M. "QSAR of phenolic compounds: statistical and artificial neural network approach" *International Conference on Chemoinformatics,* Jan 22-24, 2007 at NCL, Pune, India.

Ghosh P. & Bagchi M. C.* "Usefulness of Theoretical Molecular Descriptors in QSAR Studies of Nitrofuranyl Amides as Novel Anti-tuberculosis Agents", *International Conference on Chemoinformatics*, Jan 22-24, 2007 at NCL, Pune, India.

Madhumita Patra & Chhabinath Mandal "Comparative study of different ligand binding ability of Siglec-7 using molecular modeling techniques and structural analysis." National Conference on Resent Development in Carbohydrate Chemistry (CARBO-XXI), Delhi, November 26 -29, 2006.

Madhumita Patra & Chhabinath Mandal "Search for binding site using different computational tools." International symposium on computational biology & bioinformatics (ISBB06), Bhubaneshwar, December, 15-17, 2006.

Archana Pan, Ipsita Chanda, Jayprokas Chakrabarti and Chitra Dutta "A look into the genome and proteome composition of *Bdellovibrio bacteriovorous*, the enigmatic predator" at International Conference on Chromosomes to Neurons on 12^{th} -14^{th} Jan, 2007 at SINP, Kolkata.

Sandip Paul, Sabyasachi Das, Sumit K. Bag and Chitra Dutta "Analysis of Gene and Protein Architectures of Extremely Halophilic Microorganisms - Molecular Signature of Hypersaline Adaptation" at "Incob2006" on 18^{th}-20^{th} Dec, 2006 at Hotel Asok, New Delhi.

Sandip Paul, Sabyasachi Das, Sumit K. Bag and Chitra Dutta "Analysis of Gene and Protein Architectures of Extremely Halophilic Microorganisms - Molecular Signature of Hypersaline Adaptation" at International Conference on Chromosomes to Neurons on 12^{th} -14^{th} Jan, 2007 at SINP, Kolkata.

Sumit K. Bag, Sandip Paul, Sabyasachi Das and Chitra Dutta "SPAST - A novel software tool for analysis of trends in molecular evolution" at "Incob2006" on 18^{th}-20^{th} Dec, 2006 at Hotel Asok, New Delhi.

Reema Bhattacharya and Debasish Bhattacharyya, 'Characterization of cysteine protease bromelain in presence of detergents' -National Symposium on Biophysics: Trends in Biomedical Research, Indian Biophysical Society, New Delhi 13 -15^{th} Feb. 2007, pp 27.

Nupur Sengupta, Amrita Brahma and Debasish Bhattacharyya 'UDP-galactose 4-epimerase from K. *fragilis*: Substrates impart different effects on the enzyme during turnover', National Symposium on Biophysics: Trends in Biomedical Research, Indian Biophysical Society, New Delhi 13 - 15th Feb. 2007, pp 55.

Somnath Mondal and Debasish Bhattacharyya 'Purification and partial characterization of two L-amino acid oxidase isoforms from Russell's viper venom: Kinetic evidence of multiple binding sites for substrate analogues' National Symposium on Biophysics: Trends in Biomedical Research, Indian Biophysical Society, New Delhi 13-15th Feb. 2007, pp 113.

R.S.K. Vijayan, Nanda Ghoshal, "Three- Dimensional QSAR and Pharmacophore Model for Specific ligand Recognition at the Benzodiazepine Binding site of GABAA Receptor." International conference on Bioinformatics, December 18-20th, 2006, New Delhi, Poster no 291.

Savita Bhutoria, Nanda Ghoshal "Pharmacophoric hypothesis for Binding of Convulsant Butyrolactones To GABAA Receptor" The 4th Congress of Federation of Asian-Oceanian Neuroscience Societies (FAONS), November 30 - December 2, 2006, Hong Kong, Page 130, No. P-C143.

Sandeep Chhabra and Nanda Ghoshal "3-D QSAR Studies For The Prediction of Antileishmanial Activity of Substituted Acridines Based on Different Alignment Methods", *International Conference of Chemoinformatics*, Jan 22-24, 2007 at NCL, Pune, INDIA, Poster No. 6.

Savita Bhutoria, Nanda Ghoshal, "Interaction of Some Anticonvulsant Compounds to GABAA Receptor - A 3D QSAR Analysis Approach". *International Conference of Chemoinformatics*, Jan 22-24, 2007 at NCL, Pune, INDIA, Poster No. 26.

Pooja Sharma, Nanda Ghoshal "Structure Based Pharmacophore Generation and 3D-QSAR Analysis of Benzothiazol-2-yl-Acetonitrile Pyrimidne Core Based Derivatives As Potent C-JUN N-Terminal Kinase-3 Inhibitors", *International Conference of Chemoinformatics*, Jan 22-24, 2007 at NCL, Pune, INDIA, Poster No. 22. (Won best Poster Award).

Conferences/Symposium/Workshops

Dr. Krishnananda Chattopadhyay attended Workshop on structure and dynamics of biomolecules, S. N. Bose National Centre for Basic Sciences, Kolkata 700098 on Dec 03-08, 2007

Publications

INFECTIOUS DISEASES & IMMUNOLOGY

Ganguly, A., Das, B. B., Sen, N., Roy, A., Bose Dasgupta, S. and Majumder, H. K. 'Leish Man' topoisomerase I: an ideal chimera for unraveling the role of the small subunit of unusual bi-subunit topoisomerase I from *Leishmania donovani*. *Nucleic Acids Res.* **34:** 6286-6297, 2006.

Sen, N., Das, B. B., Ganguly, A., Banerjee, B., Sen, T. and Majumder, H. K. *Leishmania donovani*: intracellular ATP level regulates apoptosis-like death in luteolin induced dyskinetoplastid cells. *Exp. Parasitol*. **114:** 204-214, 2006.

Chaudhuri, P., Majumder, H. K. and Bhattacharya, S. Synthesis, DNA binding, and *Leishmania* topoisomerase inhibition activities of a novel series of anthra[1,2-d]imidazole-6,11-dione derivatives. *J. Med. Chem.* **50:** 2536-2540, 2007.

Das, B. B., Bose Dasgupta, S., Ganguly, A., Mazumder, S., Roy, A, Majumder, H. K. *Leishmania donovani* bi-subunit topoisomerase I gene fusion leads to an active enzyme with conserved type IB enzyme function. *FEBS J.* **274:** 150-163, 2007.

Sen, N., Banerjee, B., Das, B. B., Ganguly, A., Sen, T., Pramanik, S., Mukhopadhyay, S. and Majumder, H. K. Apoptosis is induced in leishmanial cells by a novel protein kinase inhibitor withaferin A and is facilitated by apoptotic topoisomerase I DNA complex. *Cell Death Differ.* **14:** 358-367, 2007.

Sen, N., Banerjee, B., Das, B. B., Ganguly, A., Sen, T., Pramanik, S., Mukhopadhyay, S. and Majumder, H. K. *Leishmania donovani*. Dyskinetoplastid cells survive and proliferate in the presence of pyruvate and uridine but do not undergo apoptosis after treatment with camptothecin. *Exp. Parasitol.* **115:** 215-219, 2007.

Mukherjee, S., Ukil, A. and Das, P. K. Immunomodulatory peptide from cystatin, a natural cysteine protease inhibitor, using leishmaniasis as model macrophage disease. *Antimicrob. Agents Chemother.* **51:** 1700-1707, 2007.

Dutta, A., Mandal, D., Mondal, N. B., Banerjee, S., Sahu, N. P. and Mandal, C. Racemoside A, a steroidal saponin, from *Asparagus racemosus* induces programmed cell death in *Leishmania donovani* promastigotes J. *Med. Microbiol.* **56:** 1196-1204, 2007.

Dutta, A., Bandyopadhyay, S., Mandal, C. and Chatterjee, M. Aloe vera leaf exudate induces a caspase independent cell death in *Leishmania donovani promastigotes J. Med. Microbiol*. **56:** 629-636, 2007.

Dutta, A., Mandal, G., Mandal, C. and Chatterjee, M. *In vitro* antileishmanial activity of Aloe vera leaf exudate: a potential herbal therapy in leishmaniasis. *Glycoconj. J.* **24:** 81-86.

Ratha, J., Majumdar, K. N., Mandal, S. K., Bera, R., Sarkar, C., Saha, B., Mandal, C., Saha, K. D., Bhadra, R. A sphingolipid rich lipid fraction isolated from attenuated *Leishmania donovani* promastigote induces apoptosis in mouse and human melanoma cells in vitro. *Mol. Cell. Biochem.* **290:** 113-123, 2006.

Ansar, W., Mukhopadhyay nee Bandyopadhyay, S., Chowdhury, S., Habib, Sk. H. and Mandal, C. Role of C-reactive protein in complement-mediated hemolysis in malaria. *Glycoconj. J.* **23:** 233-240, 2006.

Mookerjee Basu, J., Mookerjee, A., Sen, P., Bhaumik, S., Sen, P., Banerjee, S., Naskar, K., Choudhuri, S. K., Saha, B., Raha, S. and Roy S. Sodium antimony gluconate induces generation of reactive oxygen species and nitric oxide via phosphoinositide 3-kinase and mitogen-activated protein kinase activation in *Leishmania donovani*-infected macrophages. *Antimicrob. Agents Chemother.* **50:** 1788-1797, 2006.

Mookerjee, A., Mookerjee Basu, J., Dutta, P., Majumder, S., Bhattacharyya, S., Biswas, J., Pal, S., Mukherjee, P., Raha, S., Baral, R. N., Das, T., Efferth , T., Sa, G, Roy, S., Choudhuri, S. K. Overcoming drug-resistant cancer by a newly developed copper chelate through host-protective cytokine-mediated apoptosis. *Clin. Cancer Res.* **12:** 4339-49, 2006.

Roychoudhury, K., Dasgupta, B., Sen, P., Laskay, T., Solbach, W., De, T. and Roy S. Evidence of direct interactions between the CC-chemokines CCL3, CCL4 and CCL5 and *Leishmania* promastigotes. *Mol. Biochem. Parasitol.* **150:** 374-377, 2006.

Basu, R., Roy, S. and Walden, P. HLA-I restricted T-cell epitopes of the kinetoplastid membrane protein-11 presented by *Leishmania donovani* infected human macrophages. *J. Inf. Dis.* **195:** 1373-1380, 2007.

Ganguly, D., Paul, K., Bagchi, J., Rakshit, S., Mandal, L., Bandyopadhyay, G. and Bandyopadhyay, S. Granulocyte-macrophage colony-stimulating factor drives monocytes to CD14low CD83+ DCSIGN- interleukin-10-producing myeloid cells with differential effects on T-cell subsets. *Immunology* **121:** 499-507, 2007.

Bhowmick, S., Ravindran, R. and Ali, N. Leishmanial antigens in liposomes promote protective immunity and provide immunotherapy against visceral leishmaniasis via polarized Th1 response. *Vaccine* **25:** 6544-6556, 2007.

Chatterjee, A., Dutta, P. K. and Chowdhury, R. Effect of fatty acids and cholesterol present in bile on expression of virulence factors and motility of *Vibrio cholerae Infect. Immun*. **75:** 1946-1953, 2007.

Maiti, D., Das, B., Saha, A., Nandy, R. K., Nair, G. B. and Bhadra, R. K. Genetic organization of pre-CTX and CTX prophages in the genome of an environmental *Vibrio cholerae* non-O1, non-O139 strain. *Microbiology* **152:** 3633-3641, 2006.

Guha, M., Choubey, V., Maity, P., Kumar, S., Shrivastava, K., Puri, S. K. and Bandyopadhyay, U. Overexpression, purification and localization of apoptosis related protein from *Plasmodium falciparum. Protein Expr. Purif.* **52:** 363-372, 2007.

Kumar, S., Guha, M., Choubey, V., Maity, P. and Bandyopadhyay, U. Antimalarial drugs inhibiting hemozoin (β hematin) formation: a mechanistic update. *Life Sci*. **80:** 813-828, 2007.

Choubey, V., Maity, P., Guha, M., Kumar, S., Shrivastava, K., Puri, S. K. and Bandyopadhyay, U. Inhibition of *Plasmodium falciparum* choline kinase by hexadecyltrimethylammonium bromide: a possible antimalarial mechanism of hexadecyltrimethylammonium bromide. *Antimicrob. Agents Chemother.* **51:** 696-706, 2007.

CELL BIOLOGY & PHYSIOLOGY

Banerjee, S., Dungdung, S. R., Das, K. and Majumder G. C. Synchronous modulation of cell-surface lectin and its receptor in a homologous cell population: a novel mechanism of cellular regulation. *Exp. Cell. Res*. **312:** 2299-2308, 2006.

Joardar, A., Sen, A. K. and Das, S. Docosahexaenoic acid facilitates cell maturation and beta adrenergic transmission in astrocytes. *J. Lipid Res*. **47:** 571-581, 2006.

Dasgupta, A., Das, S. and Sarkar, P.K. Thyroid hormone promotes glutathione synthesis in astrocytes by up regulation of glutamate cysteine ligase through differential stimulation of its catalytic and modulator subunit mRNAs. *Free Rad. Biol. Med.* **42:** 617-626, 2007.

Mahata, B., Mukherjee, S., Mishra, S., Bandyopadhyay, A. and Adhya, S. Functional delivery of a cytosolic tRNA into mutant mitochondria of human cells. *Science* **314:** 471-474, 2006.

Ghose Roy, S., Mishra, S., Ghosh, G. and Bandyopadhyay, A. Thyroid hormone induces myocardial matrix degradation by activating matrix metalloproteinase. *Matrix Biol.* **26:** 269-279, 2007.

Ghosh, G., De, K., Maity, S., Bandyopadhyay, D., Bhattacharya, S., Reiter, R. J. and Bandyopadhyay, A. Melatonin protects against oxidative damage and restores GLUT- 4 expression in hyperthyroid rat heart. *J. Pineal Res.* **42:** 71-82, 2007.

Dey, D., Pal, B. C., Biswas, T., Roy, S. S., Bandyopadhyay, A., Mandal, S. K., Giri, B. B. and Bhattacharya, S. A lupinoside prevented fatty acid induced inhibition of insulin sensitivity in 3T3 L1 adipocytes. *Mol. Cell Biochem.* **300:** 149-157, 2007.

Saha, S. K., Ghosh, P., Mitra, D., Mukherjee, S., Bhattacharya, S. and Roy, S. S. Localization and thyroid hormone influenced expression of collagen II in ovarian tissue. *Cell. Physiol. Biochem.* **19:** 67-76, 2007.

Saha, S. K., Ghosh, P., Bhattacharya, S. and Roy, S. S. Procollagen synthesis is increased in hypothyroid rat ovary by a parallel and compensatory pathway. *Cell. Physiol. Biochem.* **19:** 313-322, 2007.

Dey, D., Bhattacharya, A., Roy, S. S. and Bhattacharya, S. Fatty acid represses insulin receptor gene expression by impairing HMGA1 through protein kinase Cε. *Biochem. Biophys. Res. Commun.* **357:** 474-479, 2007.

Ghosh, P., Saha, S. K., Bhattacharya, S., Bhattacharya, S., Mukherjee, S. and Roy, S. S. Tachykinin family genes and their receptors are differentially expressed in the hypothyroid ovary and pituitary. *Cell. Physiol. Biochem.* **20:** 357-368, 2007.

Banerjee, R., Sreetama, S., Saravanan, K. S., Dey, S. N. and Mohanakumar, K. P. Apoptotic mode of cell death in substantia nigra following intranigral infusion of the parkinsonian neurotoxin, MPP+ in Sprague-Dawley rats: cellular, molecular and ultrastructural evidences. *Neurochem. Res.* **32:** 1238-1247, 2007.

Saravanan, K. S., Sindhu, K. M. and Mohanakumar, K. P. Melatonin protects against rotenone-induced oxidative stress in a hemiparkinsonian rat model. *J. Pineal Res.* **42:** 247-253, 2007.

Banerjee, R., Saravanan, K. S., Chandra, G., Sen, S. and Mohanakumar, K. P. The parkinsonian neurotoxin, MPP^+ causes damages in the cell nuclei in the striatum following intrastriatal infusion in Sprague-Dawley rats. *J. Chem. Neuroanat.* **32:** 90-100, 2006.

Knaryan, V. H., Samantaray, S., Varghese, M., Srinivasan, A., Galoyan, A. A. and Mohanakumar, K. P. Synthetic bovine proline-rich-polypeptides generate hydroxyl radicals and fail to protect dopaminergic neurons against 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine-induced dopaminergic neurotoxicity in mice. *Neuropeptides* **40:** 291-298, 2006.

Sindhu, K. M., Banerjee, R., Senthilkumar, K. S., Saravanan, K. S., China Raju, B., Madhusudan Rao, J. and Mohanakumar, K. P. Rats with unilateral median forebrain bundle, but not striatal or nigral, lesions by the neurotoxins MPP^+ or rotenone display differential sensitivity to amphetamine and apomorphine. *Pharmacol.*

Biochem. Behav. **84:** 321-329, 2006

Das, T., Chattopadhyay, R., Ghosh, S., Goswami, S., Chattopadhyay, D. J., Chakravarty, B. N. and Kabir, S. N. The role of an estrogen up-regulated 64.0 kilodalton uterine fluid glycoprotein in improving fertility in women. *Fert. Sterility* **87:** 343-350, 2007.

Kumar, S., Biswas, S., Mandal, D., Roy, H. N., Chakraborty, S. N., Kabir, S. N., Banerjee, S. and Mondal, N. B. Chenopodium album seed extract: a potent sperm-immobilizing agent both *in vitro* and *in vivo*. *Contraception* **75:** 71-78, 2007.

Chakraborty, S., Bag, S., Pal, S. and Mukherjee, A. K. Structural and micro-structural characterization of bioapatite and synthetic hydroxyapatite using X-ray diffraction and FTIR techniques. *J. Appl. Cryst.* **39:** 385-390, 2006.

MOLECULAR & HUMAN GENETICS

Goswami, S. and Adhya, S. The a subunit of *Leishmania* F1 ATP synthase hydrolyzes ATP in presence of tRNA. *J. Biol. Chem.* **281:** 18914-18917, 2006.

Chatterjee, S., Home, P., Mukherjee, S., Mahata, B., Goswami, S., Dhar, G. and Adhya, S. An RNA-binding respiratory component mediated import of type II tRNAs into Leishmania mitochondria. *J. Biol. Chem.* **281:** 25270-25277, 2006.

Mahata, B., Mukherjee, S., Mishra, S., Bandyopadhyay, A. and Adhya, S. Functional delivery of a cytosolic tRNA into mutant mitochondria of human cells. *Science* **314:** 471-474, 2006.

Mukherjee, A., Paul, R. R., Chaudhuri, K., Chatterjee, J., Pal, M., Banerjee, P., Mukherjee, K., Banerjee, S. and Dutta, P. K. Performance analysis of different wavelet feature vectors in quantitation of oral precancerous condition. *Oral Oncology* **42:** 914-928, 2006.

Chatterjee, R. and Chaudhuri, K. An approach for the identification of microRNA with an application to *Anopheles gambiae. Acta Biochim Pol*. **53:** 303-309, 2006.

Ghosh, P., Banerjee, M, De Chaudhuri, S., Das, J. K., Sarma, N., Basu, A., Giri, A. K. Increased chromosome aberration frequencies in the Bowen's patients exposed to non-cancerous skin lesions individuals exposed to arsenic. *Mut. Res.-Gen. Tox.* **632:**104-110, 2007.

Das, M., Das Bhowmick, A., Sinha, S., Chattopadhyay, A., Chaudhuri, K., Singh, M. and Mukhopadhyay, K. MAOA promoter polymorphism and attention deficit hyperactivity disorder (ADHD) in Indian children. *Am. J. Med. Genet.* **141:** 637-642, 2006.

Roychoudhury, P., Ghosh, U., Bhattacharyya, N. P. and Chaudhuri, K. Activation of mitochondrial promoter P(H)-binding protein in a radio-resistant Chinese hamster cell strain associated with Bcl-2. *Biochem. Biophys. Res. Commun.* **350:** 272-276, 2006.

Roychoudhury, P., Paul, R. R., Chowdhury, R. and Chaudhuri, K. HnRNP E2 is down-regulated in human oral cancer cells and the over expression of *hnRNP E2* induces apoptosis. *Mol. Carcinog.* **46:** 198-207, 2007.

Saha, A., Mukherjee, S. and Ray, K. Improved assay for genotyping hemophilia A carriers with intron 22 dinucleotide repeat marker. *Haemophilia* **12:** 200-201, 2006.

Acharya, M., Mookherjee, S., Bhattacharjee, A., Bandyopadhyay, A. K., Thakur S. K. D., Bhaduri, G., Sen, A. and Ray K. Primary role of *CYP1B1* in juvenile onset primary open angle glaucoma. *Mol. Vis.* **12:** 399-404, 2006.

Gupta, A., Nasipuri, P., Das, S. K. and Ray, K. Simple and effective strategies for detection of allele dropouts in PCR-based diagnosis of Wilson disease. *Clin. Chem.* **52:** 1611-1612, 2006.

Chaki, M., Sengupta, M., Mukhopadhyay, A., Subba Rao, I., Majumder, P. P., Das, M., Samanta, S. and Ray, K. OCA1 in different ethnic groups of India is primarily due to founder mutations in the tyrosinase gene. *Ann. Hum. Genet*. **70:** 623-630, 2006.

Naiya, T., Biswas, A., Neogi, R., Datta, S., Misra, A. K., Das, S. K., Ray, K. and Ray J. Clinical characterization and evaluation of DYT1 gene in Indian primary dystonia patients. *Acta Neurol. Scand.* **114:** 210-215, 2006.

Aikath, D., Gupta, A., Chattopadhyay, I., Hashmi, M. A., Gangopadhyay, P. K., Das, S. K. and Ray K. Subcortical white matter abnormalities related to drug resistance in Wilson disease. *Neurology* **67:** 878-880, 2006.

Biswas, A., Gupta, A., Naiya, T., Das, G., Neogi, R., Datta, S., Mukherjee, S., Das, S. K., Ray, K and Ray J. Molecular pathogenesis of parkinson's disease: identification of causal mutations in the Parkin gene in Indian patients. *Parkin. Related Disorders*. **12:** 420-426, 2006.

Mukherjee, S., Saha, A., Kumar, P. S., Chandak, G. R., Majumadar, P. P. and Ray, K. Remarkable variation in the informativeness of RFLP markers linked to hemophilia B locus in Indian population groups: Implication in the strategy for carrier detection, *Dis. Markers.* **22:** 327-334, 2006.

Banerjee, M., Sarkar, J., Das, J. K. Mukherjee, A., Sarkar, A. K., Mondal, L. K. and Giri, A. K. Polymorphism in the ERCC2 codon 751 is associated with arsenic-induced premalignant hyperkeratosis and significant chromosomal aberrations. *Carcinogenesis* **28:** 672-676, 2007.

De Chaudhuri, S., Mahata, J., Das, J. K., Mukherjee, A., Ghosh, P., Sau, T. J., Mondal, L., Basu, S., Giri, A. K. and Roychoudhury, S. Association of specific p53 polymorphisms with keratosis in individuals exposed to arsenic through drinking water in West Bengal, India. *Mut. Res.- Fund. Mol. Mech. Mut.* **601:** 102-112,2006.

Usha, R., Guhathakurta, S., Ghosh, S., Sinha, S., Chatterjee, A., Ahmed, S., Roy Choudhury, S., Gangopadhyay, P. K., Ghosh, S. and Singh, M. Serotonin transporter promoter variants: analysis in Indian autistic and control population. *Brain Res.* **1092:** 28-35, 2006.

Sengupta, S., Chakrabarti, S., Roy, A., Panda, C. K. and Roychoudhury, S. Inactivation of *hMLH1* and *hMSH2* in HNSCC tumors and leukoplakia by promoter hypermethylation and its relation with MIN phenotype. *Cancer* **109:** 703-712, 2007.

Mondal, G., Sengupta, S., Panda, C. K., Gollin, S. M., Saunders, W. S. and Roychoudhury, S. Overexpression of Cdc20 leads to impairment of the spindle assembly checkpoint and aneuploidization in oral cancer. *Carcinogenesis* **28:** 81-92, 2007.

Reshmi, S. C., Roychoudhury, S., Yu, Z., Feingold, E., Potter, D., Saunders, W. S. and Gollin, S. M. Inverted duplication pattern in anaphase bridges confirms the breakage-fusion-bridge (BFB) cycle model for 11q13 amplification. *Cytogenet. Genome Res.* **116:** 46-52, 2007.

DRUG DEVELOPMENT, DIAGNOSTICS & BIOTECHNOLOGY

Saha, D., Acharya, D., Roy, D., Shrestha, D. and Dhar, T. K. Simultaneous enzyme immunoassay for the screening of aflatoxin B1 and ochratoxin A in chili samples. *Anal. Chim. Acta* **584:** 343-349, 2007.

Saha, D., Acharya, D., Roy, D. and Dhar, T. K. Filtration-based tyramide amplification technique--a new simple approach for rapid detection of aflatoxin B1. *Anal. Bioanal. Chem.* **387:** 1121-1130, 2007.

Saha, D., Acharya, D. and Dhar, T. K. Method for homogeneous spotting of antibodies on membranes: application to the sensitive detection of ochratoxin *A. Anal. Bioanal. Chem.* **385:** 847-854, 2006.

Saha, M., Jaisankar, P., Das, S., Sarkar, K. K., Roy, S., Besra, S. E., Vedasiromoni, J. R., Ghosh, D., Sana, B. and Mukherjee, J. Production and purification of a bioactive substance inhibiting multiple drug resistant bacteria and human leukemic cells from a salt-tolerant marine *Actinobacterium sp*. isolated from the Bay of Bengal. *Biotechnol. Lett.* **28:** 1083-1088, 2006.

Dasgupta, S., Debnath, A., Saha, A., Giri, B., Tripathi, G., Vedasiromoni. J. R., Gomes, A. and Gomes, A. Indian black scorpion (*Heterometrus bengalensis*, koch) venom induced antiproliferative and apoptogenic activity against leukemic cell lines. *Leukemia Res.* **31:** 817-825, 2006.

Debnath, A., Chatterjee, U., Das, M., Vedasiromoni, J. R. and Gomes, A. Venom of Indian monocellate cobra and Russell's viper show anticancer activity in experimental models. *J. Ethnopharmacol*. **111:** 681-684, 2007.

Das, N. and Mukherjee, M. Cultivation of *Pleurotus ostreatus* on weed plants. *Biores. Technol.* **98:** 2723-2726, 2007.

Malakar, D., Dey, A. and Ghosh, A. K. Protective role of S-adenosyl-L-methionine against hydrochloric acid stress in *Saccharomyces cerevisiae. Biochem. Biophys*. *Acta,* General. **1760:** 1298-1303, 2006.

Mandal, M., Saha, S., Ghosh, A. K. and Majumder, G. C. Identification and characterization of a sperm motility promoting glycoprotein from buffalo blood serum. *J. Cellular Physiol***. 209:** 353-362, 2006.

Ganguly, K., Kundu, P., Banerjee, A., Reiter, R. J. and Swarnakar, S. Hydrogen peroxide-mediated downregulation of matrix metalloprotease-2 in indomethacin-induced acute gastric ulceration is blocked by melatonin and other antioxidants. *Free Rad. Biol. Med.* **41:** 911-925, 2006.

Kundu, P., Mukhopadhyay, A. K., Patra, J., Banerjee, A., Berg, D.E. and Swarnakar, S. cag negative *Helicobacter pylori* strain infection upregulates matrix metalloproteinase-9 expression and activity in mice. *J. Biol. Chem*. **281:** 34651-34662, 2006.

Swarnakar, S., Mishra, A., Ganguly, K. and Sharma, A. V. Matrix metalloproteinase-9 activity and expression is reduced by melatonin during prevention of ethanol-induced gastric ulcer in mice. *J. Pineal Res.* **43:** 56-64, 2007.

Kumar, A. and Chattopadhyay, S. DNA damage protecting activity and antioxidant potential of pudina extract. *Food Chem.* **100:** 1377-1384, 2007.

Mukherjee, S., Chowdhury, S., Ghorai, S., Pal, S. and Khowala, S. Cellobiase from *Termitomyces clypeatus*: Activity and secretion in presence of glycosylation inhibitors. *Biotechnol. Lett.* **28:** 1773-1778, 2006.

Mandal, A. K., Das, S., Basu, M. K., Chakrabarti, R. N. and Das, N. Hepatoprotective Activity of liposomal flavonoid against arsenite-induced liver fibrosis. *J. Pharmacol. Exp. Ther.* **320:** 994-1001, 2007.

CHEMISTRY

Ray, A., Manoj, K., Bhadbhade, M. M., Mukhopadhyay, R. and Bhattacharjya, A. Cu (I) catalyzed cycloaddition of constrained azidoalkynes: access to 12 to 17?membered monomeric triazolophanes incorporating furanoside rings. *Tetrahedron Lett.* **47:** 2775-2778, 2006.

Roy, A., Achari, B. and Mandal, S. B. An easy access to spiroannulated glyco-oxetane, -thietane and -azetane rings: synthesis of spironucleosides. *Tetrahedron Lett.* **47:** 3875-3879, 2006.

Sahabuddin, Sk., Roy, A., Drew, M. G. B., Roy, B. G., Achari, B. and Mandal, S. B. Sequential ring closing metathesis and nitrone cycloaddition on glucose derived substrates: a divergent approach to analogues of spiroannulated carbanucleosides and conformationally locked nucleosides. *J. Org. Chem.* **71:** 5980-5992, 2006.

Roy, B. G., Roy, A., Achari, B. and Mandal, S. B. A simple one-pot entry to cyclic ethers of varied ring sizes from diols via phosphonium ion induced iodination and base catalyzed Williamson etherification. *Tetrahedron Lett.* **47:** 7783-7787, 2006.

Roy, B. G., Maiti, J. K., Drew, M. G. B., Achari, B. and Mandal, S. B. Carbanucleosides: synthesis of both enantiomers of 2-(6-chloropurin-9-yl)-3,5-bishydroxymethyl cyclopentanol from D-glucose. *Tetrahedron Lett*. **47:** 8821-8825, 2006.

Roy, B. G., Jana, P. K., Achari, B. and Mandal, S. B. A short and efficient synthesis of 5-hydroxymethylcyclopent-2-enol from D-glucose and its elaboration to the carbanucleoside (-)-carbovir. *Tetrahedron Lett*. **47:** 1563-1566, 2007.

Dey, S., Nandi, D.; Pradhan, P. K ,Giri, V. S. and Jaisankar P. Indium trichloride cata- lyzed one-pot synthesis of highly substituted furans. *Tetrahedron Lett.* **48:** 2573-2575, 2007.

Saha, M., Jaisankar, P., Das, S., Sarkar, K., Roy, S., Besra, S. E., Vedasiromani, J. R. Ghosh, D., Sana, B. and Mukherjee, J. Production and purification of an antimicrobial substance inhibiting multiple drug resistant bacteria from a salt-tolerant marine actinobacterium isolated from the Bay of Bengal. *Biotechnol. Lett.* **28:** 1083-1088. 2006.

Bindu, P. C., Jaisankar, P., Hauer, F., Gutzeit, H. O. and Kundu, S. C. Biological relevance of host plant-derived terpenoid in the cocoons of the tropical tasar silkworm *Antheraea mylitta. Biochem. Syst. Ecol.* **34:** 698-704, 2006.

Giri, P., Hossain, M. and Suresh Kumar, G. Molecular aspects on the specific interaction of cytotoxic plant alkaloid palmatine to poly(A). *Intl. J. Biol. Macromol*. **39:** 210-221, 2006.

Islam, Md. M., Sinha R. and Suresh Kumar, G. RNA binding small molecules: studies on t-RNA binding by cytotoxic plant alkaloids berberine, palmatine and comparison to ethidium. *Biophys. Chem.* **125:** 508–520, 2007.

Bhadra, K., Maiti, M. and Suresh Kumar, G. Molecular recognition of DNA by small molecules: AT base pair specific intercalative binding of cytotoxic plant alkaloid palmatine. *Biochim. Biophys. Acta-General* **1770:** 1071-1080, 2007.

Mandal, D, Banerjee, S., Mondal, N. B., Chakravarty, A. K. and Sahu N. P. Steroidal saponins from the fruits of *Asparagus racemosus*. *Phytochemistry* **67:** 1316-1321, 2006.

Lala, S., Gupta, S., Sahu, N. P., Mandal, D., Mondal, N. B., Moulik, S. P. and Basu, M. K. Critical evaluation of the therapeutic potential of basic acid incorporated in oil-in-water microemulsions and poly-D,L-lactide nanoparticles against experimental leishmaniasis. *J. Drug Target.* **14:** 171-179, 2006.

Bhattacharyya, K., Kar, T., Bocelli, G., Banerjee, S. and Mondal, N. B. Farnesiaside, a new diterpene glycoside. *Acta Crystallographica* **62:** 4007-4009, 2006.

Kumar, S., Biswas, S., Mandal, D., Roy, H. N., Chakraborty, S., Kabir, S. N., Banerjee, S. and Mondal, N. B. *Chenopodium album* seed extract: a potent sperm-immobilizing agent both *in vitro* and *in vivo*. *Contraception* **75:** 71-78, 2007.

Banerjee, M., Mukhopadhyay, R., Achari, B. and Banerjee, A. K. An improved synthetic route to angularly functionalized hydrofluorene derivatives through Pd(0)-catalysed heck reaction. *Synthesis* **8:** 1263-1272, 2006.

Dey, D., Pal, B. C., Biswas, T., Roy, S. S., Bandyopadhyay, A., Mandal, S. K., Giri, B. B. and Bhattacharya, S. A lupinoside prevented fatty acid induced inhibition of insulin sensitivity in 3T3 L1 adipocyte. *Mol. Cell. Biochem*. **300:** 149-157, 2007.

Neogi, A., Majhi, T. P., Ghosh, S., Mukherjee, A. K. and Chattopadhyay, P. Sequential Baylis-Hillman reaction and radical cyclization of furanos derivatives: expeditious approach to enantiopure benzofused nine-membered oxacycles *Tetrahedron* **62:** 12003-12010, 2006.

Neogi, A., Majhi, T. P., Mukhopadhyay, R., and Chattopadhyay, P. Palladium mediated intramolecular aryl amination on furanose derivatives: an expedient approach to the synthesis of chiral benzoxazocine derivatives andtricyclic nucleosides. *J. Org. Chem*. **71:** 3291-3294, 2006.

STRUCTURAL BIOLOGY & BIOINFORMATICS

Samaddar, S., Mandal, A. K., Mondal, S. K., Sahu, K., Bhattacharyya, K. and Roy, S. Solvation dynamics of a protein in the pre-molten globule state *J. Phys. Chem. B.* **110:** 21210-21215, 2006.

Bagchi, M. C., Mills, D. and Basak, S. C. Quantitative structure-activity relationship (QSAR) studies of quinolone antibacterials against *M. fortiutum* and *M. smegmatis* using theoretical molecular descriptors. *J. Mol. Model* **13:** 111-120, 2007.

Majumder, S., Patra, M. and Mandal C. Search for fucose binding domains in recently sequenced hypothetical proteins using molecular modeling techniques and structural analysis. *Glycoconj. J*. **23:** 253-259, 2006.

Patra, M. and Mandal C. Search for glucose/galactose-binding proteins in newly discovered protein sequences using molecular modeling techniques and structural analysis. *Glycobiology* **16:** 959-968, 2006.

Patra, M., Majumder, S., and Mandal C. Structural studies on mannose-selective glycoprotein receptors using molecular modeling techniques. *Glycoconj. J.* **23:** 243-251, 2006.

Das, S., Paul, S. Bag, S. K. and Dutta, C. Analysis of *Nanoarchaeum equitans* genome and proteome composition: indications for hyperthermophilic and parasitic adaptation. *BMC Genomics.* **7:** 186, 2006.

Maiti, G., Mandal, S. and Bhattacharyya, D. Purification and characterization of 6 kDa PLA2 from Russells viper venom. *J. Chromatog. B.* **845:** 232-243, 2007.

Mandal, S. and Bhattacharyya, D. Ability of a small basic protein from Russell's viper venom to induce renal tubular necrosis in mice. *Toxicon* **50:** 236-250, 2007.

Sharma, P. and Ghoshal, N. Exploration of a binding mode of benzothiazol-2-yl- acetonitrile pyrimidine core base derivatives as potent c-Jun N-terminal kinase-3 inhibitors and 3D-QSAR analyses. *J. Chem. Inform. Modeling*. **46:** 1763-1774, 2006.

Sharma, P., Chhabra, S., Rai, N. and Ghoshal, N. Exploration of rate-limiting conformational state for 5-[(7-chloro-4-quinolinyl)amino]-3-[(alkylamino)methyl][1,1¢-biphenyl]-2-ols and Nˆ-oxides (tebuquine analogues) for antimalarial activity using molecular shape analysis and molecular field analysis studies. *J. Chem. Inform. Modeling*. **47:** 1087-1096, 2007.

Dolai, S., Yadav, R. K., Datta, A. K. and Adak, S. Effect of thiocyanate on the peroxidase and pseudocatalase activities of Leishmania major ascorbate peroxidase. *Biochim. Biophys. Acta-General* **1770:** 247-256, 2007.

PUBLICATIONS

Publications (2006-2007) at a glance

Total Number of Publications	**...**	**109**
Average Impact Factor	**...**	**3.60**

BOOKS/REVIEWS/POPULAR ARTICLES

INFECTIOUS DISEASES & IMMUNOLOGY

Majumder H. K. Executive Editor of the book entitled *Drug targets in kinetoplastid parasites*, Landes Biosciences Publishers, Springer, USA, 2007.

Das, B. B., Sengupta, T., Ganguly, A. and Majumder, H. K. Topoisomerases of kinetoplastid parasites: why so fascinating? *Mol. Microbial.* **62:** 917-27, 2006.

Mukhopadhyay nee Bandyopadhyay, S. and Mandal, C. Targeting glycoproteins or glycolipids and their metabolic pathways for anti-parasite therapy. *In: Drug targets in kinetoplastid parasites*, (Ed.: H. K. Majumdar), Landes BioScience Publishers, Springer, USA, 2007.

Ghosh, S., Bandyopadhyay, S., Mukherjee, K., Mallick, A., Pal, S., Mandal, C., Bhattacharya D. K. and Mandal, C. O-acetylation of sialic acids is required for the survival of lymphoblasts in childhood acute lymphoblastic leukemia (ALL): A review *Glycoconj. J.* **24:** 17-24.

Mukhopadhyay nee Bandyopadhyay, S. and Mandal, C. Glycobiology of *Leishmania donovani. Indian J. Med. Res.* **123:** 203-220, 2006.

CELL BIOLOGY & PHYSIOLOGY

Saha, S. K., Ghosh, P., Mitra, D., Konar, A., Bhattacharya, S., Mukherjee S. and Roy, S. S. Ovarian tissue remodelling: the role of extra cellular matrix. *In: Hormone Biotechnology* (Ed.: S. K. Maitra), Daya Publishing House, New Delhi, India pp. 179-188 2007.

Bhattacharya, S., Dey, D. and Roy, S. S. Molecular mechanism of insulin resistance. *J. Biosci.* **32:** 405-413, 2007.

Das, S. and Mohanakumar, K. P. (Eds.) A handbook of neurochemical techniques for the neuroscientists. *YOU CAN DO IT Series*, Indian Institute of Chemical Biology, pp. 1-107. 2007.

Mohanakumar, K. P. Basic research: the root to pharmaceutical industry. *In: West Bengal pharma review*, Express Pharma, pp. 33-35, 2006.

Mohanakumar, K. P. Reviewed the book 'Drug discovery for nervous system diseases, John Wiley & Sons Inc., Hoboken, New Jersey, USA (Ed. F. F. Hefti), *J. Chem. Neuroanat.* **32,** 79-80 2006.

Kabir S. N. and Bandyopadhyay, S. Ovarian dysfunction under galactose toxicity. *In: Hormone biotechnology*, (Ed.: S. K. Mitra), Daya Publishing House, Delhi, India, pp. 384-398, 2007.

Kabir, S. N., Bandyopadhyay, S. and Banerjee, S. Impaired galactosylation of FSH – a pathway to ovarian resistance in galactosemia. *In: Recent advances in molecular and integrative physiology*, (Ed.: B. Bandyopadhyay), Physiology Department, Raja Peary Mohan College, Hooghly, West Bengal, India, pp. 26-31, 2007.

MOLECULAR & HUMAN GENETICS

Das, S. K. and Ray K. Wilson's Disease: An update, *Nature Clinical Practice Neurology,* **2:** 482-493, 2006.

Ray K, and Gupta A. Single Nucleotide Polymorphism: A Novel Genomic Tool for the Pharmaceutical Industries. *In: Biodiversity and Biotechnology* (Eds.: S. Ray and A. K. Ray), New Central Book Agency Pvt Ltd), Kolkata, India, 272-285, 2006.

DRUG DEVELOPMENT, DIAGNOSTICS & BIOTECHNOLOGY

Goswami, S., Sett, S., Annalakshmi, C., Kar, S. K. and Das, P. K. *In vitro* screening of Indian medicinal plants in search of gastric anti-HCl secreting principle(s). Proceedings of the UGC-sponsored national seminar on Medicinal Plants: Its present status, prospects & conservation (Ed. A. P. Ray), Department of Botany, Midnapore College, West Bengal, India, pp. 91-100, 2006.

Das, P. K., Goswami, S., Annalakshmi, C., Panda, N., Banerjee, S., Sahu, N. P. and Achari, B. *Woodfordia fruticosa*: traditional uses and recent findings. *J. Ethnopharmacol.* **110:** 189-199, 2007.

CHEMISTRY

Pramanick, S., Banerjee, S., Achari, B. and Mukhopadhyay, S. Phytochemicals from the Genus *Andrographis. In: Recent Progress in Medicinal Plants Phytomedicines*. Studium Press LLC, *Houston, USA*. **16:** 339-387, 2006.

External Funding

INFECTIOUS DISEASES & IMMUNOLOGY

Principal investigator : Dr. H. K. Majumder
Project title : Leishmania donovani unusual bi-subunit topoisomerase I: Solving the new twist in topoisomerase research related to evolution, functional conservation and preferential sensitivity to the specific inhibitors of type IB family
Funding Agency : DBT, Govt. of India
Total Funds : Rs. 21.98 lakhs only
Duration : June 9, 2006 to June 8, 2009

Principal investigator : Dr. Pijush K. Das
Project title : Cyclic nucleotide signaling in the infectivity of an eukaryotic intracellular pathogen like *Leishmania*
Funding Agency : DST, Govt. of India
Total Funds : Rs. 22.00 lakhs
Duration : November 2006 to November 2009

Principal investigator : Dr. (Mrs.) Nahid Ali
Project Title : Therapeutic efficacy of positively charged liposomes against *Leishmania donovani*.
Funding Agency : ICMR, Govt. of India.
Total Funds : Rs. 26.21 lakhs
Duration : 2004-2007

Principal Investigator : Dr. Tripti De
Co-Investigator : Dr. Syamal Roy
Project Title : Protective efficacy of galactose terminal glycoconjugates of *Leishmania donovani*.
Funding Agency : DST
Total Fund : Rs. 20 lakhs
Duration : April 2006-March 2009

Principal Investigator : Dr. (Mrs.) Mridula Misra
Project Title : Development of New Radiopharmaceuticals for Nuclear Brain Imaging: Pharmacokinetics and Mechanism of action
Funding Agency : ICMR, Govt. of India
Total Fund : Rs. 20 lakhs
Duration : 2005 - 2008

Principal Investigator : Dr. Mita Chatterjee Debnath
Project Title : Kit formulation of thiolate complexes of technetium -99m using S-thiomethyl as a novel protecting group for SH-containing ligands.
Funding Agency : ICMR
Total Funds : Rs. 1.99 lakhs
Duration : February 2007 - October 2007

Principal Investigator : Dr. Mita Chatterjee Debnath
Project Title : Rapid Diagnosis of myocardial cell damage by a novel radiotracer.
Funding Agency : DST
Total Funds : Rs. 19.86 lakhs
Duration : August 2004-Nov 2007

CELL BIOLOGY & PHYSIOLOGY

Principal Investigator : Dr. Sib Sankar Roy (Co-PI)
Project Title : DBT multi-Institutional project, entitled "Development of a Herbal Drug for Non-Insulin Dependent Diabetes mellitus"
Funding Agency : Department of Biotechnology
Total Funds : Rs 58.27 lakhs
Duration : November 2004 up to October 2007

Principal Investigator : Dr. Sib Sankar Roy
Project Title : Herbal based preparations for degenerative disorders: Diabetes mellitus type II (NIDDM) with emphasis on insulin sensitization and Herboprint-A tool for standardization of herbal medicine"
Funding Agency : NMITLI
Total Funds : Rs. 40 lakhs
Duration : April 2002 to September 2007

Principal Investigator : Dr. K P Mohanakumar
Project Title : In vitro targeting and functional characterization of ES cell derived dopaminergic neurons and exploration of their therapeutic potential.
Funding Agency : Department of Biotechnology
Total Funds : Rs. 65.80 lakhs
Duration : 2004-2007

Principal Investigator : Dr. Sumantra Das
Project Title : Limbal stem cell culture and transplantation of cultivated corneal epithelial stem cells in ocular surface disorders
Funding Agency : Department of Biotechnology
Total Funds : Rs. 24.456 lakhs
Duration : November 2005 upto October, 2008

MOLECULAR & HUMAN GENETICS DIVISION

Principal investigator : Dr. Samit Adhya
Project Title : Role of two proteins in mitochondrial tRNA import
Funding Agency : DST
Total Funds : Rs. 15.68 lakhs
Duration : August 2005 - July 2008

Principal investigator : Dr. Kunal Roy
Project Title : Novel molecular diagnostics for eye diseases and low vision enhancement devices
Funding Agency : NMITLI
Total Fund : Rs. 32.6 lakhs
Duration : April 2003 - Sept. 2006

Principal investigator : Dr. Keya Chowdhury
Project Title : Malignant potentiality of precancerous oral submucous fibrosis and its association with expression of collagen types
Funding Agency : DST
Total Fund : Rs. 19.23 lakhs
Duration : 2005-2008

Principal investigator : Dr. A. K. Giri
Project title : Fogarty International Training Programme
Funding Agency : University of California, Berkeley, USA
Total Fund : $ 40,550
Duration : 2005-2007

Principal investigator : Dr. Samir Kumar Dutta
Project title : Biochemical characterization and molecular cloning of a chymotrypsin/ trypsin inhibitor from winged bean seeds
Funding agency : DST, Govt. of India, New Delhi
Total Fund : Rs. 18.51 lakhs
Duration : 2003-2007

DRUG DEVELOPMENT, DIAGNOSTICS & BIOTECHNOLOGY

Principal Investigator : Dr.(Mrs.) Aparna Gomes
Co-investigator : Dr.(Mrs.) Minati Das
Project Title : Experimental evaluation of snake venom as an antineoplastic agent.
Funding Agency : ICMR, Govt. of India
Total Fund : Rs. 6.163 lakhs
Duration : 2003 - 2006

Principal Investigator : Dr.(Mrs.) Aparna Gomes
Co-investigator : Dr.J.R.Vedasiromoni
Project Title : Evaluation of scorpion venom as an anticancer agent.
Funding Agency : DST, Govt. of India
Total Fund : Rs.15.16 lakhs
Duration : 2004 - 2007

Principal Investigator : Dr. A. K. Ghosh
Project Title : Standardisation and Identification (if possible) of ingredients present in TRASINA
Funding Agency : Dey's Medical Stores (Mfg.) Ltd
Total Fund : Rs. 7.08 lakhs
Duration : July, 2003 - June, 2006

Principal Investigator	:	Dr. Snehasikta Swarnakar
Project Title	:	Effect of omeprazole on regulation of matrix and remodeling of extracellular matrix in gastroduodenal ulcer.
Funding Agency	:	ICMR, Govt. of India
Total Fund	:	Rs. 18.70 lakhs
Duration	:	2005 - 2008

Principal Investigator	:	Dr. Sharmila Chattopadhyay
Project Title	:	Role of Glutathione as a signaling molecule
Funding agency	:	DST, Govt. of India.
Total Cost	:	Rs. 23 lakhs
Duration	:	2007-2010

Principal Investigator	:	Dr. Sharmila Chattopadhyay
Project Title	:	Indian Medicinal Plants to combat kala-azar
Funding agency	:	ICMR, Govt. of India.
Total Cost	:	Rs. 28.5 lakhs
Duration	:	2007-2010

Co-coordinator	:	Dr. Pratap K. Das
Project Title	:	Chemical standardization and biological evaluation with a view to increase efficacy of herbal medicines
Funding Agency	:	DST, Govt. of India & Dey's Medical Mfg. Co. Ltd.
Total Fund	:	Rs. 45.81 lakh (IICB Component)
Duration	:	2005-2008

Principal Investigator	:	Dr Suman Khowala
Project Title	:	Role of glycosylation on production, activity & secretion of cellobiase in *T. clypeatus*
Funding agency	:	DBT, Govt. of India.
Total Cost	:	Rs. 25 lakhs
Duration	:	2003-2006

CHEMISTRY

Principal Investigator	:	Dr. Asish Kumar Sen
Project Title	:	Immunomodulation and anti-microbicidal activity: effect of Bael (*Aegle marmelos*) exudate gum, and mucilage and other polysaccharides from semi-ripe Bael fruit.
Funding Agency	:	DBT, Govt. of India.
Total Fund	:	Rs. 18.62 lakhs
Duration	:	2004-2007

Principal Investigator	:	Dr. Asish Kumar Sen
Project Title	:	Chemical Characterization and modification of coir fiber for enhanced longevity, and their physico-chemical studies
Funding Agency	:	Coir Board, Govt. of India..
Total Fund	:	Rs. 29.48 lakhs
Duration	:	Nov 2006 - October 2009

Principal investigator : Dr. B. C. Pal
Project Title : Development of herbal drug for non-insulin Dependent Diabetes mellitus
Funding agency : DBT
Total Fund : Rs. 8.12 lakhs (IICB component)
Duration : 2004 -2007

Principal Investigators : Dr. N.B. Mondal and Santu Bandyopadhyay
Co-Investigator : Dr. Sukdeb Banerjee
Project Title : Evaluation of anilidoquinoline analogue as an oral anti leishmanial drug in animal models.
Funding agency : DBT, Govt. of India
Total Fund : Rs. 33.15 lakhs
Duration : 2003-2006.

Principal Investigators : Dr. V. S. Giri and Dr. A. K. Banerjee
Project Title : Identification and Optimization of Lead Molecules for Development as Anti-cancer Agents
Funding Agency : DST and Dabur Research Foundation
Total Fund : Rs. 30.704 lakhs
Duration : 2005-2006

Principal Investigator : Dr. P. Jaisankar
Project Title : Development of Chiral Catalysts for Asymmetric Organic Synthesis
Funding Agency : DST
Total Fund : Rs. 6.5 lakhs (IICB component)
Duration : 2006-2009

STRUCTURAL BIOLOGY & BIOINFORMATICS

Principal Investigator : Prof. Siddhartha Roy
Project Title : Structural basis of specific operator recognition and engineering for novel specificity
Funding Agency : DST, Govt. of India
Total Funds : Rs. 33.00 lakhs
Duration : 2005-2008

Principal Investigator : Prof. Siddhartha Roy
Project Title : Development of anti-viral agents against Chandipura virus
Funding Agency : Department of Biotechnology, (Govt. of India) New Delhi.
Total Funds : Rs. 10.07 lakhs
Duration : 2005-2008

Principal Investigator : Dr. M. C. Bagchi
Project Title : Indo-Slovenian project on QSAR of antituberculosis drugs: a comparison of statistical and neural net methods
Funding Agency : National Institute of Chemistry, Slovenia and DST, Govt. of India
Total Funds : 3120 EURO (Slovenian side) + Rs. 0.88 lakhs (Indian side)
Duration : 2005-2006

Principal Investigator	:	Dr. M. C. Bagchi
Project Title	:	Anti-tuberculosis Drug Design by Calculated Molecular descriptors: A QSAR Approach.
Funding Agency	:	Department of Biotechnology, (Govt. of India) New Delhi.
Total Funds	:	Rs. 12.07 lakhs
Duration	:	2006-2009

Principal Investigator	:	Dr. Chitra Dutta
Project Title	:	Establishment of Sub-DIC at IICB
Funding Agency	:	Department of Biotechnology, (Govt. of India) New Delhi.
Total Funds	:	Rs. 53 lakhs
Duration	:	2002-2007 (extended up to 2012)

Principal investigator	:	Dr Debasish Bhattacharyya
Project title	:	Regulation of activity and assembly of multineric proteins
Funding agency	:	DST
Total funds	:	Rs. 20.00 lakhs
Duration	:	2006 (December) - 2009 (November)

Principal investigator	:	Dr. Saumen Datta
Project title	:	Structural Insights into the Type III Secretion System (TTSS) of Pathogenic Bacteria
Funding agency	:	DST
Total funds	:	Rs. 22.51 lakhs
Duration	:	2007-2010

Principal Investigator	:	Dr. Subrata Adak
Co-Investigator	:	Dr. Alok K. Datta
Project Title	:	Molecular and functional characterization of ascorbate peroxidase from *Leishmania major.*
Funding Agency	:	DST, Govt. of India
Total Funds	:	Rs. 21.77 lakhs
Duration	:	2006-2009

Doctorates from the Institute

Name of Ph.D. awarded candidate	*Name of the Supervisor / Division*

INFECTIOUS DISEASES & IMMUNOLOGY

Dr. Nilkantha Sen	Dr. H. K. Majumder / Infectious Diseases & Immunology
Dr. Benu Brata Das	Dr. H. K. Majumder / Infectious Diseases & Immunology
Dr. Snigdha Mukherjee	Dr. P. K. Das / Infectious Diseases & Immunology
Dr. Labanya Mandal	Dr. Santu Bandopadhyay / Infectious Diseases & Immunology
Dr. Dipyaman Ganguly	Dr. Santu Bandopadhyay / Infectious Diseases & Immunology
Dr. (Mrs.) Srabanti Rakshit	Dr. Santu Bandopadhyay / Infectious Diseases & Immunology
Dr. Diganta Maiti	Dr. Rupak Bhadra / Infectious Diseases & Immunology

CELL BIOLOGY & PHYSIOLOGY

Dr. A K Navneet	Dr. S. S. Roy and Prof. S. Bhattacharya / Cell Biology & Physiology
Dr. Sundararajan Raja	Dr. A. Bandopadhyay / Cell Biology & Physiology
Dr. Gautam Ghosh	Dr. A. Bandopadhyay / Cell Biology & Physiology
Dr. Sutapa Banerjee	Dr. S. N. Kabir / Cell Biology & Physiology

MOLECULAR & HUMAN GENETICS

Dr. Saibal Chatterjee	Dr. Samit Adhya / Molecular & Human Genetics
Dr. Moulinath Achary	Dr. Kunal Ray / Molecular & Human Genetics
Dr. Saibal Mukherjee	Dr. Kunal Ray / Molecular & Human Genetics
Dr. Madhubanti Sarkar	Dr. Keya Chowdhury / Molecular & Human Genetics

DRUG DEVELOPMENT, DIAGNOSTICS & BIOTECHNOLOGY

Dr. Papiya Ghosh	Dr. J.R.Vedasiromoni & Dr. Smita Mitra / Drug Development, Diagnostics & Biotechnology
Dr. Ramdhan Majhi	Dr. A.K. Ghosh / Drug Development, diagnostics & Biotechnology

Name of Ph.D. awarded candidate	*Name of the Supervisor / Division*

CHEMISTRY

Dr. Subir Ghorai	Dr. Anup Bhattacharjya / Chemistry
Dr. Sarbendu Maiti	Dr. Ashis K. Banerjee / Chemistry
Dr. Sujaya Sengupta	Dr. Ashis K. Banerjee /Chemistry
Dr. Aniruddha Nandi	Dr. Partha Chattopadhyay / Chemistry
Dr. Bikash Pal	Dr. V. S. Giri / Chemistry
Dr. Prasun Kanti Pradhan	Dr. V. S. Giri / Chemistry
Dr. Goutam Biswas	Dr. Anup Bhattacharjya / Chemistry
Dr. Jhimli Sengupta	Dr. Anup Bhattacharjya / Chemistry
Dr. Debraj Mukherjee	Dr. Partha Chattopadhyay / Chemistry
Dr. Seikh Sahabuddin	Dr. S. B. Mandal / Chemistry
Dr. Ashim Roy	Dr. S. B. Mandal / Chemistry
Dr Subhankar Tripathi	Dr. S. B. Mandal / Chemistry
Dr. Amrita Chatterjee	Dr. Pronab K. Bhattacharjya / Chemistry
Dr. Mainak Banerjee	Dr. Ashis K. Banerjee / Chemistry
Dr.(Mrs.) Moumita Gupta	Dr. B. C. Pal / Chemistry

STRUCTURAL BIOLOGY & BIOINFORMATICS

Dr. Subhagata Ghosh	Dr. Chitra Dutta / Structural Biology & Bioinformatics
Dr. Gargi Maity	Dr. Debasish Bhattacharyya / Structural Biology & Bioinformatics
Dr. Sangeeta Nath	Dr. Debasish Bhattacharyya / Structural Biology & Bioinformatics

Honours and Awards

INFECTIOUS DISEASES & IMMUNOLOGY

Dr. H. K. Majumder

* Sir Jnan Chandra Ghosh Memorial Award by Science Association of Bengal for outstanding contribution in promotion of science in the State in 2007.

* Working Chairman of the West Bengal State Council of Science & Technology, Govt. of West Bengal.

* Nominated by the Council of the National Academy of Sciences, India to act a Member of Fellowship Scrutiny Committee for the Fellowship of the Academy (FNASc) for Biological Sciences for the year 2003-2004.

* Nominated by the Council of the Indian National Academy of Sciences (FNA) to act as a member of the Sectional Committee on Animal Sciences, (Section-VII) for the year 2006-2009.

* Member of the Research Council of Vector Control Research Centre (VCRC), ICMR, Pondicherry, Tamil Nadu (2004-2007).

* Member of the Board of Studies of West Bengal University of Technology (WBUT).

Dr. Pijush K. Das

* Elected Fellow of the Indian National Science Academy (FNA), New Delhi 2006.

* Member of the American Association of Immunologists.

* Departmental Core Committee Member of the Recruitment and Assessment Board (RAB) of CSIR.

* Member of Board of Studies of Calcutta University.

* Reviewer of National & International journals.

Dr. (Mrs.) Nahid Ali

* Received Prof. A.N. Bhaduri Memorial Lecture Award.

CELL BIOLOGY & PHYSIOLOGY

Dr. K.P. Mohanakumar

* CSIR Senior Research Fellow Mritunjay Pandey was awarded the T Desiraju memorial prize for the best Oral presentation prize during the Young Investigators Colloquium at the Kolkata Neuroscience Meeting 2007 and 3rd International Symposium on "Neurodegeneration and Neuroprotection" from 8th to 9th January, 2007.

* Reviewer of Brain Research (USA), Behavioural Brain Research (Germany), European Neuropsychopharmacology (Netherlands), Nitric Oxide (USA), Neuroscience Research (Ireland), Neurochemical Research (USA), Life Science (England), Journal of Diabetes and Its Complications (USA), The Journal of Agricultural Science (UK), BMC Neuroscience (England), Journal of Neuroscience Research (USA), Journal of Tissue Research (India), Indian Journal of Pharmacology (India), Current Science (India), Indian Journal of Biochemistry and Biophysics (India).

Dr. S.N. Kabir

* Federation of Obstetrics and Gynaecological Society of India (FOGSI) award in Reproductive Endocrinology (2007).

Dr. Sumantra Das

* CSIR Senior Research Fellow Mausam Ghosh was awarded the best poster award during 6th IBRO-Associate School of Neuroscience and 1st Neuroscience Orientation Summer Program, at Neuroscience Research Center, Shaheed Beheshti University of Medical Sciences and Tarbiat Modares University, Tehran, Iran from August 26th to September 21st, 2006.

* Reviewer of a number of International journals.

MOLECULAR & HUMAN GENETICS

Dr. Samit Adhya

* Member, Board of Examiners and Ph.D. Committee, Calcutta University

* Member, Research Advisory Committee, Monovikas Kendra, Calcutta

* Member, Project Advisory Committee, National Institute of Immunology, New Delhi

Dr. Keya Chaudhuri

* Mr. Arunava Bandyopadhaya (SRF with Dr. Keya Chaudhuri) won Dr Manasi Ram Prize for best poster presentation at the 29th All India Cell Biology Conference Lucknow, January 18-20,2006.

* Ms. Susri Roychoudhury (Guha) (RA with Dr. Keya Chaudhuri) won Prafulla Kumar Memorial Award for best platform presentation at the 'International Conference on Free Radicals and Antioxidants in Health, Disease and Radiation & 5th Annual Conference of Society for Free Radical Research', Science City, Kolkata, January 16-18, 2006.

Dr. Kunal Ray

* Elected a member of Human Genome Organization (HUGO), London, 2006.

* Elected Fellow of West Bengal Academy of Science & Technology, 2007.

* Reviewer for the following journals: (i) Archives of Ophthalmology, (ii) BMC Genetics, (iii) BMC Molecular Biology, (iv) Investigative Ophthalmology & Visual Sciences, (v) Journal of Biosciences, (vi) Molecular Vision.

* A graduate student, Ms. Ashmia Bhattacharyya received the best poster award at the 32nd Annual Meeting of the Indian Society of Human Genetics (ISHG) and International Symposium on "Deconstructing Human Diseases: The Genomic Advantage (14th-16th February, 2007) at Science City, Kolkata.

* A graduate student, Ms. Moumita Chaki received Young Scientist Award at the 32nd Annual Meeting of the Indian Society of Human Genetics (ISHG) and International Symposium on "Deconstructing Human Diseases: The Genomic Advantage (14th-16th February, 2007) at Science City, Kolkata.

Dr. Susanta Roychoudhury

* Elected a member of Human Genome Organization (HUGO), London, 2006.

* Elected a member of Guha Research Conference, 2006.

DRUG DEVELOPMENT, DIAGNOSTICS & BIOTECHNOLOGY

Dr. J. R. Vedasiromoni

* Member, Editorial Board of Indian Journal of Pharmacology.

* Elected as Vice-President of Indian Pharmacological Society for 2006

Dr. Snehasikta Swarnakar

* National Science Day award for outstanding contribution to science, research, education and social activities by The Science Association of Bengal, Kolkata, 2006.

Dr. Pratap K. Das

* Nominated as the Member of the Sectional Committee of the Section of Biological Sciences (New Biology) for of the 95th Indian Science Congress Association 2007-08.

CHEMISTRY

Dr. A.K. Sen (Jr.)

* Elected as Hon. Secretary of the Association of Carbohydrate Chemists & Technologists (India) 2007-2008.

Dr. G. Suresh Kumar

* Ms Kakali Bhadra, SRF was awarded poster award to present a paper at the Fifth East Asian Biophysics Symposium and Forty-Fourth Annual Meeting of the Biophysical Society of Japan, November 12-16 2006, Okinawa, Japan.

STRUCTURAL BIOLOGY & BIOINFORMATICS

Prof. Siddhartha Roy

* Awarded "J.C. Bose Fellowship" by Ministry of Science & Technology, Govt.India.

* Elected fellow of West Bengal Academy of Science & Technology, Kolkata.

Dr. Chhabinath Mandal

* Served as reviewer for BMC Structural Biology.

* Served as reviewer for *In Silico* Biology.

* Served as a moderator of West Bengal University of Technology.

Dr. Chitra Dutta

* Awarded "Stree Shakti Science Sanman-2006".

* Member, Board of Studies, School of IT, Bengal Engineering and Science University, (Deemed University) Shibpur.

* Member, Board of Studies, Dept. of Biotechnology, National Institute of Technology (Deemed University) Durgaprur, W.B.

* Reviewer, Nucleic Acids Research, BMC Genomics, BMC Evolutionary Biology, Microbiology etc.

* Member, Editorial Board, International Journal of Soft Computing & Bioinformatics.

Sl. No.	EMPLOYEE'S NAME	EMP. ID	DESIGNATION

Staff List of IICB as on 31. 03. 2007

Staff Strength at a Glance

Director	…	…	1
Scientist, Gr. IV	…	…	77
Engineer	…	…	5
Technical, Gr. III	…	…	54
Technician, Gr. II	…	…	30
Helper, Gr. I	…	…	17
Ministerial Officer	…	…	14
Ministerial Staff	…	…	63
Gr. D (Non-Technical)	…	…	20
Canteen Staff	…	…	10
TOTAL	**…**	**…**	**291**

Detailed Staff List

Scientific and Technical

Sl. No.	EMPLOYEE'S NAME	EMP. ID	DESIGNATION
1.	Prof. Siddhartha Ray	489	DIRECTOR
2.	Dr. H. K. Majumdar	23	SCIENTIST G
3.	Dr. Samit Adhya	37	DO
4.	Dr. Pijush K. Das	40	DO
5.	Dr. Anup Bhattacharya	30	SCIENTIST F
6.	Dr. V. S. Giri	39	DO
7.	Sri Debashish Pal	43	DO
8.	Dr. K. P. Mohanakumar	77	DO
9.	Dr. Tarun K. Dhar	63	DO
10.	Dr. S. B. Mondal	76	DO
11.	Dr. (Mrs.) M. Mukherjee	47	DO
12.	Dr. A. K. Sen (Jr)	65	DO
13.	Dr. (Mrs.) Chitra Mandal	60	DO

Sl. No.	EMPLOYEE'S NAME	EMP. ID	DESIGNATION
14.	Dr. J. R. Vedasiromoni	53	DO
15.	Dr. B. C. Pal	64	DO
16.	Dr. Anil K. Ghosh	68	DO
17.	Dr. P. K. Bhattacharya	56	DO
18.	Dr. Syamal Roy	93	DO
19.	Dr. (Mrs.) Keya Chowdhury	83	DO
20.	Dr. Sumantra Das	87	DO
21.	Sri Ajoy Kr. Banerjee	85	DO
22.	Dr. Partha Chattopadhyay	81	DO
23.	Dr. S. B. Mukhopadhyay	80	DO
24.	Dr. Ashish Kr. Sen (Sr)	55	SCIENTIST E II
25.	Dr. Aparesh Bhattacharya	59	DO
26.	Dr. Manish Ch. Bagchi	78	DO
27.	Dr. Shyamal Kumar Dana	86	DO
28.	Dr. Ashok Kumar Giri	402	DO
29.	Dr. (Mrs.) Smita Mitra	71	DO
30.	Dr. U. S. Chowdhury	84	DO
31.	Dr. S. N. Kabir	90	DO
32.	Dr. (Mrs.) Chitra Dutta	95	DO
33.	Dr. (Mrs.) Aparna Gomes	91	DO
34.	Dr. Santu Bandopadhyay	97	DO
35.	Dr. Debashish Bhattacharya	96	DO
36.	Dr. Nirmalendu Das	100	DO
37.	Dr. (Mrs.) Nahid Ali	103	DO
38.	Dr. G. Suresh Kumar	105	DO
39.	Dr. Susanta Roychowdhury	98	DO
40.	Dr. (Miss) Moonmoon Bhowmik	110	DO
41.	Dr. Kunal Ray	415	DO
42.	Dr. Samir Kr. Dutta	111	DO
43.	Dr. Sukdeb Bandopadhyay	102	DO
44.	Dr. Nirup Bikash Mondal	107	DO
45.	Dr. (Mrs.) Tuli Biswas	109	DO
46.	Dr. P. Jaisankar	112	DO

Sl. No.	EMPLOYEE'S NAME	EMP. ID	DESIGNATION
47.	Dr. (Mrs.) Rukhshana Chowdhury	115	DO
48.	Dr. S. N. Chakraborty	94	DO
49.	Dr. Ram Chandra Yadav	154	DO
50.	Dr. Ranjan Mukhopadhyay	114	DO
51.	Dr. Asish Kr. Banerjee	116	DO
52.	Dr. (Mrs.) Nanda Ghoshal	119	DO
53.	Dr. (Miss) Chhanda Mitra	51	SCIENTIST E I
54.	Dr. Pratap Kr. Das	62	DO
55.	Sri U. K. Barua	464	DO
56.	Dr. Binayak Das	108	DO
57.	Dr. Tushar Kanti Chakraborty	99	DO
58.	Dr. (Mrs.) Padma Das	117	DO
59.	Dr. (Mrs.) Suman Khowala	118	DO
60.	Dr. Arun Bandyopadhyay	445	DO
61.	Dr. (Mrs.) S. R. Dungdung	120	DO
62.	Dr. Rupak Kr. Bhadra	124	DO
63.	Dr. Tanmoy Mukherjee	125	DO
64.	Dr. Soumen Datta	503	DO
65.	Dr. Chinmay Chowdhury	520	DO
66.	Dr. Uday Bandopadhyay	521	DO
67.	Dr. K. N. Chattopadhyay	523	DO
68.	Dr. Mrinal Kanti Ghosh	524	DO
69.	Dr. Arindam Banerjee	526	DO
70.	Mrs. N. V. M. Khalko	122	DO
71.	Dr. (Mrs.) Debjani Mondal	123	DO
72.	Dr. (Mrs.) Tripti De	433	DO
73.	Dr. Aditya Konar	441	DO
74.	Dr. Sibsankar Ray	443	DO
75.	Dr. Bijon Kumar Ghosh	404	SCIENTIST C
76.	Dr. (Mrs) Sarmila Chattopadhyay	447	DO
77.	Dr. Subrata Adak	472	DO
78.	Dr. (Miss) Snehasikta Swarnakar	473	DO

Sl. No.	EMPLOYEE'S NAME	EMP. ID	DESIGNATION
79.	Dr. (Mrs.) Mridula Misra	142	TECHNICAL OFFICER E II
80.	Dr. (Mrs.) Krishna Das Saha	143	DO
81.	Sri H. N. Roy	152	DO
82.	Dr. (Mrs.) S. E. Besra	145	DO
83.	Sri Tapan Kumar Mukherjee	140	TECHNICAL OFFICER E I
84.	Sri Kalyan Kr. Sarkar	147	DO
85.	Sri Sailendra Nath Dey	148	DO
86.	Sri Kalyanmay Dutta	153	DO
87.	Sri Ujjal Baran Sarkar	155	DO
88.	Sri Tapan Kr. Chakraborty	159	DO
89.	Sri A. K. Das	151	DO
90.	Sri Subodh Kr. Roy	156	DO
91.	Dr. (Mrs) Mita Chatterjee Debnath	432	DO
92.	Sri S. K. Sahoo	163	DO
93.	Sri D. P. Das	130	EXECUTIVE ENGINEER/Gr. III(5)
94.	Sri Sandip Saha	494	DO
95.	Sri Susanta Ray	514	ASSISTANT EXEC. ENGINEER
96.	Sri B. Jayakumar	517	DO
97.	Mrs. Nirali Bage	466	JUNIOR ENGINEER, GR. I
98.	Dr. S. Majumdar	164	TECHNICAL OFFICER C
99.	Sri Mohan Lal Jana	167	DO
100.	Dr. Prashanta Kr. Chakraborty	169	DO
101.	Dr. Kalidas Paul	168	DO
102.	Sri Shekhar Ghosh	467	DO
103.	Sri A. K. Bairagi	165	DO
104.	Sri Samir Kr. Roy	171	DO
105.	Dr. Ashok Kumar Dasgupta	172	DO
106.	Sri Narayan ch. Ghosh	499	DO
107.	Sri Surajit Mohan Roy	166	DO
108.	Sri Gautam Gupta	170	DO
109.	Sri Binayak Pal	448	DO
110.	Mrs. Aparna Laskar	449	DO
111.	Sri Kshudiram Naskar	162	TECHNICAL OFFICER B

Sl. No.	EMPLOYEE'S NAME	EMP. ID	DESIGNATION
112.	Dr. Sankar Kumar Maitra	174	DO
113.	Dr. Ardhendu Kr. Mandal	175	DO
114.	Dr. Tapas Sarkar	177	DO
115.	Dr. Subhagata Ghosh Miss	179	DO
116.	Sri Arupesh Majumdar	180	DO
117.	Sri Rajat Bandopadhyay	181	DO
118.	Dr. Ramdhan Majhi	184	DO
119.	Sri R. N. Mandi	185	DO
120.	Sri P. Gangopadhyay	186	DO
121.	Sri Asish Mullick	187	DO
122.	Mrs. Dipika Roy	188	DO
123.	Dr. (Mrs) Gayatri Tripathi	462	DO
124.	Mrs. Purnima Chatterjee	173	DO
125.	Mrs. Banasri Das	176	DO
126.	Sri Diptendu Bhattacharya	178	DO
127.	Sri E. Padmanaban	496	DO
128.	Sri Sekhar Mukherjee	477	DO
129.	Sri Pratap Ch. Kayal	182	DO
130.	Sri Utpal Halder	157	TECHNICAL OFFICER A
131.	Sri Sandip Chowdhury	411	SENIOR TECHNICAL ASSISTANT
132.	Dr. (Mrs) Shampa Sarkar	461	JUNIOR TECHNICAL ASSISTANT
133.	Mrs. Arti Khetrapaul	463	DO
134.	Sri Swapan Kr. Mondal	465	DO
135.	Sri Jishu Mandal	495	DO
136.	Sri Debashis Banik	513	DO
137.	Sri Sandip Chakraborty	516	DO
138.	Sri Asutosh Mukherjee	193	TECHNICIAN GR. II(4)
139.	Sri Ajoy Kr. Pramanik	195	DO
140.	Sri M. B. Malakar	219	DO
141.	Sri S. K. Basak	220	DO
142.	Sri Phelaram Dhank	309	DO
143.	Sri Goutam Malik	224	DO
144.	Sri D. K. Ghosh	233	TECHNICIAN GR. II(3)

Sl. No.	EMPLOYEE'S NAME	EMP. ID	DESIGNATION
145.	Sri Gopal Ch. Sarkar	234	DO
146.	Sri P. K. Chanda	236	DO
147.	Sri S. N. Mondal	237	DO
148.	Sri S. K. Prodhan	239	DO
149.	Sri S. C. Das	241	DO
150.	Sri S. R. Tudu	251	DO
151.	Sri Swapan Kumar Naskar	244	DO
152.	Md. Ayub Shah	344	DO
153.	Sri Sheo Shankar Verma	242	DO
154.	Sri Tapas Chowdhury	246	DO
155.	Sri Pradip Mondal	383	DO
156.	Sri A. K. Sen	478	DO
157.	Sri Tarak Prasad Nandi	247	DO
158.	Mrs. Sutapa Ganguly	248	DO
159.	Sri Sanjib Biswas	249	DO
160.	Sri R. P. Gorh	250	DO
161.	Sri Sarit K. Sarkhel	245	TECHNICIAN GR. II(2)
162.	Sri Nishikanta Naskar	252	DO
163.	Sri Pallab Mukherjee	253	DO
164.	Sri Ranjit Das	345	DO
165.	Sri Abhijit Paul	450	DO
166.	Sri Anirban Manna	410	DO
167.	Sri Samir Majumder	426	TECH. ,GR,II(1)
168.	Sri R. Mahato	258	HELPER GR. I(4)
169.	Sri Tapan Kumar Mukherjee	267	DO
170.	Sri Sunil Nath	272	DO
171.	Sri R. N. Jana	274	DO
172.	Sri Prahlad Das	275	DO
173.	Sri Bhaskar Basu	440	DO
174.	Sri Ramdas Ravidas	346	DO
175.	Sri Brihaspati Das	347	DO
176.	Sri Shyamal Das	279	HELPER GR. I(3)
177.	Sri Sasthi C. Sil	356	DO

Sl. No.	EMPLOYEE'S NAME	EMP. ID	DESIGNATION
178.	Sri Madan Halder	479	DO
179.	Sri Amerika Das	280	DO
180.	Sri Nimai Charan Prodhan	282	DO
181.	Mrs. Uma Biswas	455	HELPER GR. I(2)
182.	Sri Ashoke Sardar	501	HELPER GR. I(I)
183.	Sri Ram Kumar Sarkar	502	DO
184.	Sri Shyamal Nath	519	DO

Administration

Sl. No.	EMPLOYEE'S NAME	EMP. ID	DESIGNATION
1.	Sri S. K. Chaudhuri	497	ADMINISTRATIVE OFFICER
2.	Sri S. K. Das	498	F & A OFFICER
3.	Sri Yantindra Chauhan	484	STORES & PURCHASE OFFICER
4.	Sri U. S. Das	515	STORES & PURCHASE OFFICER
5.	Sri Subhas Ch. Dutta	290	SR. SECURITY OFFICER
6.	Sri Kausik Bhattacharjee	492	SECTION OFFICER (GENERAL)
7.	Sri H. N. Bonia	483	DO
8.	Sri Siddhartha Dey	485	DO
9.	Mrs. Shampoo Sengupta	525	DO
10.	Mrs. Rubai Roy	436	SECTION OFFICER (S&P))
11.	Sri Asim Kr. Jha	518	SECTION OFFICER (F&A))
12.	Sri Basudev Bhattacharya	459	PRIVATE SECRETARY
13.	Sri S. K. Chhatui	312	DO
14.	Sri D. P. Thakur	493	DO
15.	Sri K. C. Das	302	ASSISTANT (GENERAL) GR. I
16.	Mrs. Ratnabali Adhikari	304	DO
17.	Sri D. R. Chakraborty	306	DO
18.	Mrs. Anjana Mandi	308	DO
19.	Sri Kanu Mondal	392	DO
20.	Sri Ratan Bage	397	DO
21.	Mrs. Sanhita Ganguly	427	DO
22.	Mrs. Monalisa Mukhopadhyay	428	DO
23.	Mrs. Rita Sikdar	326	DO
24.	Miss Lily Das	330	DO

Sl. No.	EMPLOYEE'S NAME	EMP. ID	DESIGNATION
25.	Sri P. K. Saha	468	DO
26.	Sri Paritosh Purkait	339	DO
27.	Mrs. Indira Kundu	331	ASSISTANT (GENERAL) GR. II
28.	Sri R. N. Hansda	334	DO
29.	Sri Prem Singh	335	DO
30.	Sri D. K. Kisku	340	DO
31.	Md. M. Ahmed	360	DO
32.	Sri Alok Ray	396	DO
33.	Sri Paresh Sarkar	409	DO
34.	Sri Sujit Kr. Majumdar	416	DO
35.	Mrs. Mahua Bhattacharjee	419	DO
36.	Sri Prabir Kr. Das	418	DO
37.	Sri Atanu Maitra	417	DO
38.	Sri Tapan Das	460	DO
39.	Sri Jayanta Pal	510	ASSISTANT (GENERAL) GR. III
40.	Sri Tarun Kr. Sinha Roy	508	DO
41.	Sri Raju Pal	507	DO
42.	Sri Ranjit Debnath	509	DO
43.	Sri Saugata Das	511	DO
44.	Sri Sukhendu Biswas	512	DO
45.	Sri Mrinal K. Ghosh	299	ASSISTANT (F & A) GR. I
46.	Sri A. K. Chanda	327	DO
47.	Mrs. Banani Dutta	476	DO
48.	Sri Sanjoy Mukhopadhyay	343	DO
49.	Mrs. P. L. Saha	332	ASSISTANT (F & A) GR. II
50.	Sri Asit K. Roy	336	DO
51.	Sri M. K. Dutta	338	DO
52.	Sri Vishal Agarwal	506	ASSISTANT (F&A) GR. III
53.	Sri Tapan Kr. Mitra	320	ASSISTANT (S & P) GR. I
54.	Sri Panchanan Naskar	322	DO
55.	Sri A. B. S. Roy	328	DO
56.	Sri R. L. Bhattacharya	329	DO
57.	Sri Bisweswar Das	342	ASSISTANT (S & P) GR. II

Sl. No.	EMPLOYEE'S NAME	EMP. ID	DESIGNATION
58.	Sri Rajib Roy	420	DO
59.	Mrs. Bula Pal	363	DO
60.	Sri Pradipta Sarkar	505	ASSISTANT (S&P) GR. III
61.	Sri Arnab Sen	504	DO
62.	Mrs. Ambalika Nag	321	SR. HINDI TRANSLATOR
63.	Sri Mangala Prasad Banerjee	469	SR. STENOGRAPHER (ACP)
64.	Sri Debdas Guhathakurta	313	DO
65.	Sri Nikhil Kumar Das	315	DO
66.	Sri Sankar Prasad Dutta	316	DO
67.	Sri Dipak Kr. Guin	318	DO
68.	Sri Asim Roy	323	SR. STENOGRAPHER
69.	Mrs. Pratima Banerjee	324	DO
70.	Sri Shankar Bhakta	325	DO
71.	Sri Rabindranath Das	393	DO
72.	Sri Saibal Giri	405	DO
73.	Sri Gautam Saha	453	JR. STENOGRAPHER
74.	Sri Sudip Ghosh	454	DO
75.	Sri Sankar Santra	490	DO
76.	Smt Moumita Majumdar	491	DO
77.	Sri U. N. Mandi	358	RECORD KEEPER
78.	Sri Ashok Ram	348	GR-D (NT) (UPGRADED under ACP)
79.	Sri Bideshi Nayak	349	DO
80.	Sri N. N. Prodhan	354	DO
81.	Sri Sambhu Raul	351	GR-D (NT) (UPGRADED)
82.	Sri Suresh Balmiki	353	DO
83.	Sri Nanda Lal Routh	352	DO
84.	Sri S. K. Banik	361	DO
85.	Mrs. Chaina Devi Nayak	366	DO
86.	Sri Kailash Chandra Nayak	365	DO
87.	Mrs. Gita Ghosh	364	DO
88.	Mrs Soma Devi Sharma	401	DO
89.	Sri Gopal Ch. Mandal	412	DO
90.	Sri Asit Mitra	413	DO

Sl. No.	EMPLOYEE'S NAME	EMP. ID	DESIGNATION
91.	Sri Janmanjoy Midya	431	DO
92.	Sri Pasupati Midya	430	DO
93.	Sri P. C. Dehury	414	GROUP-D (NT)
94.	Sri Shyamal Kr. Ghosal	423	DO
95.	Sri Tapan Sarkar	424	DO
96.	Sri Manoranjan Adhikary	425	DO
97.	Sri Dinesh Mehali	451	DO
98.	Sri Tarun Dutta	367	ASSTT. MANAGER-CUM-STORE KEEPER
99.	Sri Amal Dutta	369	COUPON CLERK
100.	Sri Balaram Panda	368	HALWAI-CUM-COOK
101.	Sri Sudhangshu Halder	373	TEA MAKER
102.	Sri Bimal Das	372	BEARER
103.	Sri Ashok Sadhukhan	371	BEARER
104.	Sri Badal Haldar	370	BEARER
105.	Sri Jagabandhu Biswas	374	WASH BOY
106.	Sri Mantu Das	376	SWEEPER
107.	Sri Nirapada Halder	375	SWEEPER

Retirement List from April 01, 2006 to March 31, 2007

Sl. No.	Name of the Staff Member	Designation	Date of Retirement
1.	Sri Puran Bahadur	Helper, Gr. I	31.05.2006
2.	Dr. A.K. Chakraborty	Scientist, F	31.05.2006
•••	•••	Tech. Officer, Gr. III	30.06.2006
4.	Dr. (Miss) J. Bhattacharjee	Scientist, E II	31.07.2006
5.	Dr. P.K. Dutta	Scientist, F	31.07.2006
6.	Sri A.M. Dhank	Technician, Gr. II	31.08.2006
7.	Sri Abdul Kader	Technician, Gr. II	31.10.2006
8.	Dr. (Mrs) R. Bandyopadhyay	Scientist, F	30.11.2006
9.	Dr. Alok K. Dutta	Scientist, F	30.11.2006
10.	Dr. Chhabinath Mandal	Scientist, E II	30.11.2006
11.	Dr. Dwijen Sarkar	Scientist, F	30.11.2006
12.	Sri Asit Sen	Assistant (G), Gr. I	30.11.2006
13.	Sri D.K. Dutta	Assistant (G), Gr. I	31.12.2006
14.	Sri Sanjoy Basu	Scientist, F	28.02.2007

New Appointment from April 01, 2006 to March 31. 2007

Sl. No.	Name of the Staff Member	Designation	Date of Appointment
1.	Dr. Soumen Datta	Scientist, E I	18.04.2006
2.	Sri Jayanta Pal	Assistant (G), Gr. III	15.05.2006
3.	Sri Tarun Kr. Sinharay	Assistant (G), Gr. III	15.05.2006
4.	Sri Raju Pal	Assistant (G), Gr. III	15.05.2006
5.	Sri Ranjit Debnath	Assistant (G), Gr. III	15.05.2006
6.	Sri Sugata Das	Assistant (G), Gr. III	22.05.2006
7.	Sri Sukhendu Biswas	Assistant (G), Gr. III	30.05.2006
8.	Sri Arnab Sen	Assistant (S&P), Gr. III	15.05.2006
9.	Sri Pradipta Sarkar	Assistant (S&P), Gr. III	15.05.2006
10.	Sri Vishal Agarwal	Assistant (F&A), Gr. III	15.05.2006
11.	Sri Debasish Banik	Tech. Assistant Gr. III(1)	26.06.2006
12.	Sri Susanta Kr. Roy	Asstt. Ex. Engr. Gr. III(4)	01.08.2006
13.	Sri Sandip Chakraborty	Tech. Assistant Gr. III(1)	17.08.2006
14.	Sri J. Jayakumar	Asstt. Ex. Engr. Gr. III(4)	25.08.2006
15.	Dr. Chinmoy Chowdhury	Scientist, E I	11.10.2006
16.	Sri Shyamal Nath	Helper, Gr. I(1)	12.10.2006
17.	Dr. Uday Bandyopadhyay	Scientist, E I	04.12.2006
18.	Dr. K.N. Chattopadhyay	Scientist, E I	22.12.2006
19.	Dr. Mrinal K. Ghosh	Scientist, E I	20.02.2007
20.	Dr. Arindam Banerjee	Scientist, E I	15.03.2007

Research Council 2006-2007 of IICB

Prof. M. R. S. Rao, Chairman
President, Jawaharlal Nehru Centre for Advanced Scientific Research
Jakkur P.O., Bangalore – 560 064
Fax : 080 2208 2766 / 2360 2468
Tel : 080 2362 2762 / 2293 2461 / 2360 0491 (O) ; 080 2351 9131 (Res.)
E-mail : mrsrao@jncasr.ac.in; mrsrao@biochem.iisc.ernet.in

Dr. Santanu Bhattacharya, Member
Department of Organic Chemistry
Indian Institute of Science, Bangalore – 560 012
Fax : 080 2360 0529 ; Tel : 080 2293 2664 / 2293 2777 (O) ; 080 2360 1944 (Res.)
E-mail : sb@orgchem.iisc.ernet.in

Dr. Seyed E. Hasnain, Member
Director, Centre for DNA Engineering & Diagnostics
ECIL Road, Nacharam, Hyderabad – 500 076
Fax : 040 2715 5610 / 2715 5479
Tel : 040 2715 5604 / 2715 5605 (O) ; 040 2715 1350 (Res.)
E-mail : director@cdfd.org.in

Dr. K. Vijay Raghavan, Member
Director, National Centre for Biological Sciences
UAS-GKVK Campus, Bellary Road, Bangalore – 560 065
Fax : 080 2363 6675 / 2363 6662 ; Tel : 080 2363 6460 / 2363 6421-32 / 2240
E-mail : vijay@ncbs.res.in ; vijay@tifr.res.in

Prof. N. K. Mehra, Member
Professor, Dept. of Transplant Immunology & Immunogenetics
All India Institute of Medical Sciences
Ansari Nagar, New Delhi – 110 029
Fax : 011 2658 8663 / 2658 8641
Tel : 011 2658 8588 / 2659 4638 (O) ; 011 2658 8185 / 2659 4510 (Res.)
E-mail : narin98@hotmail.com ; nkmehra@medinst.ernet.in

Dr. S. K. Bhattacharya, Member
Director, National Institute of Cholera & Enteric Diseases
P-33, CIT Road, Scheme XM, Beliaghata, Kolkata – 700 010
Fax : 033 2350 5066 ; Tel : 033 2353 7519 / 2350 1176 (O) ; 033 2335 6566 (Res.)
E-mail : sujitkbhattacharya@yahoo.com ; bsujit@vsnl.net

Dr. K. N. Ganesh, Member
Scientist, National Chemical Laboratory
Pashan Road, Pune – 411 008
Fax : 020 2589 3153 ; Tel : 020 2589 3153 (O) ; 020 2589 8320 (Res.)
E-mail : kng@ems.ncl.res.in

Dr. Amit Ghosh, Member
Director, School of Biological Sciences
Indian Institute of Advanced Research
The Puri Foundation
Block 2, 1st Floor, Udyog Bhavan
Sector 11, Gandhinagar – 382 011, Gujarat
Tel : 079 2328 9050
E-mail : amitghosh24@yahoo.com

Prof. B. Bhattacharya, Member
Department of Biochemistry
Bose Institute, Centenary Building
P-1/12, CIT Scheme VII M, Kolkata – 700 054
Fax : 033 2234 3886
Tel : 033 2337 9219 / 9544 (O) ; 033 2422 3812 (Res.)
E-mail : bablu@boseinst.ernet.in

Dr. Naresh Kumar, Member
Head, RDPD
Council of Scientific & Industrial Research
Anusandhan Bhawan, 2 Rafi Marg
New Delhi - 110 001
Fax : 011 2371 0340

Prof. Siddhartha Roy, Member
Director, Indian Institute of Chemical Biology
4, Raja S. C. Mullick Road, Jadavpur, Kolkata – 700 032
Fax : 033 2473 5197
Tel : 033 2413 1157 / 2473 5368 (O) ; 033 2429 8795 / 2412 1261 (Res.)
E-mail : siddhartharoy@iicb.res.in

Dr. Pijush K. Das, Secretary
Scientist, Indian Institute of Chemical Biology
4 Raja SC Mullick Road, Jadavpur, Kolkata – 700 032
Fax : 033 2473 5197
Tel : 033 2414 0921 (O) ; 033 2476 9216 / 2475 8443 (Res.)
E-mail : pijushkdas@vsnl.com ; pijushdas@iicb.res.in

Special Permanent Invitee

Prof. Asis Datta
Director, National Centre for Plant Genome Research &
Professor of Molecular Biology & Biochemistry
School of Life Sciences, Jawaharlal Nehru University
New Delhi – 110 067
Fax : 011 2616 7394
Tel : 011 2618 7224 / 2617 2594 / 2671 5267 / 2671 4031 (O)
011 2610 6437 / 2671 5263 (Res.) ; 011 2671 4560 (L)
E-mail : ncpgr02@bol.net.in ; asisdatta@hotmail.com

Management Council 2006-2007 of IICB

Prof. Siddhartha Roy
Chairman
Director, Indian Institute of Chemical Biology
4, Raja S.C. Mullick Road, Jadavpur, Kolkata - 700 032
Phone: (033) 2473-0492/3491/3493/6793
Fax: (033) 2473 5197, 2472 3967
E-mail: director@iicb.res.in;siddhartharoy@iicb.res.in

Dr. H. S. Maiti
Director, Central Glass & Ceramic Research Institute
196, Raja S.C. Mullick Road, Jadavpur, Kolkata - 700 032
Phone: (033) 2473-5829/3469/3476-77/3496
Fax: (033) 2473 0957
E-mail: director@cgcri.res.in;hsmaiti@cgcri.res.in

Dr. K. P. Mohana Kumar
Scientist, Indian Institute of Chemical Biology
4, Raja S.C. Mullick Road, Jadavpur, Kolkata - 700 032
Phone: (033) 2473-0492/3491/3493/6793
Fax: (033) 2473 5197, 2472 3967
E-mail: mohankumar@iicb.res.in

Dr. J. Rajan Vedasiromoni
Scientist, Indian Institute of Chemical Biology
4, Raja S.C. Mullick Road, Jadavpur, Kolkata - 700 032
Phone: (033) 2473-0492/3491/3493/6793
Fax: (033) 2473 5197, 2472 3967
E-mail: vedasiromoni@iicb.res.in

Dr. (Mrs.) Tuli Biswas
Scientist, Indian Institute of Chemical Biology
4, Raja S.C. Mullick Road, Jadavpur, Kolkata - 700 032
Phone: (033) 2473-0492/3491/3493/6793
Fax: (033) 2473 5197, 2472 3967
E-mail: tulibiswas@iicb.res.in

Dr. Rupak Kr. Bhadra
Scientist, Indian Institute of Chemical Biology
4, Raja S.C. Mullick Road, Jadavpur, Kolkata - 700 032
Phone: (033) 2473-0492/3491/3493/6793
Fax: (033) 2473 5197, 2472 3967
E-mail: rupakbhadra@iicb.res.in

Dr. Sibsankar Roy
Scientist, Indian Institute of Chemical Biology
4, Raja S.C. Mullick Road, Jadavpur, Kolkata - 700 032
Phone: (033) 2473-0492/3491/3493/6793
Fax: (033) 2473 5197, 2472 3967
E-mail: sibsankar@iicb.res.in

Dr. Asoke Kumar Das Gupta
Technical Officer, Indian Institute of Chemical Biology
4, Raja S.C. Mullick Road, Jadavpur, Kolkata - 700 032
Phone: (033) 2473-0492/3491/3493/6793
Fax: (033) 2473 5197, 2472 3967
E-mail: asokedg@iicb.res.in

Finance & Accounts Officer
Indian Institute of Chemical Biology
4, Raja S.C. Mullick Road, Jadavpur, Kolkata - 700 032
Phone: (033) 2473-0492/3491/3493/6793
Fax: (033) 2473 5197, 2472 3967

Administrative Officer
Indian Institute of Chemical Biology
4, Raja S.C. Mullick Road, Jadavpur, Kolkata - 700 032
Phone: (033) 2473-0492/3491/3493/6793
Fax: (033) 2473 5197, 2472 3967

Published by
Director, Indian Institute of Chemical Biology

Published from
Indian Institute of Chemical Biology
4 Raja SC Mullick Road, Kolkata – 700 032
Phone : (033) 2473 3491 / 0492 / 3493 / 6793
Fax : (033) 2473 5197, 2472 3967
E-mail : director@iicb.res.in
Website : www.iicb.res.in

Publication Committee
Dr. Pijush K. Das (Chairman), Dr. Tanmoy Mukherjee (Convenor)
Dr. Rupak Bhadra, Dr. G. Suresh Kumar, Dr. Arupesh Majumder
Mr. Nikhil K. Das (Secretarial Assistance)

Designed and Printed by
CDC Printers Pvt. Ltd.
13, Crooked Lane, Kolkata – 700 069
Phone : 2248 8167 / 3048
E-mail : cdc@cdcprinters.co.in
Website : www.cdcprinters.co.in